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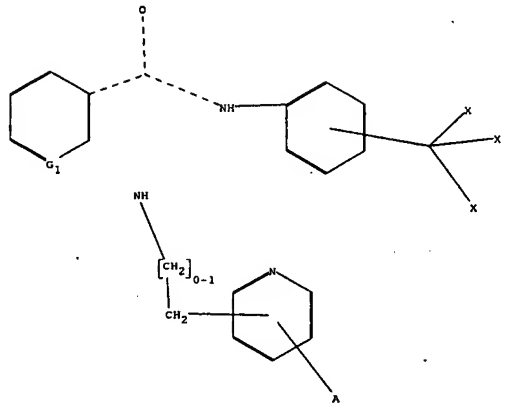

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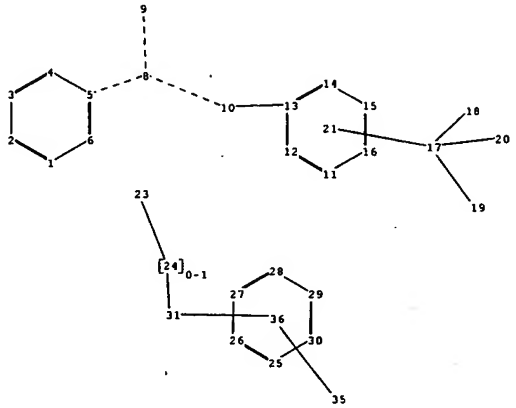

chain nodes :
8 9 10 17 18 19 20 23 24 31 35
ring nodes :
1 2 3 4 5 6 11 12 13 14 15 16 25 26 27 28 29 30
chain bonds :
5-8 8-9 8-10 10-13 17-18 17-19 17-20 23-24 24-31
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 11-12 11-16 12-13 13-14 14-15 15-16 25-26 25-30
26-27 27-28 28-29 29-30
exact/norm bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-8 8-9 8-10 10-13 17-18 17-19 17-20 23-24 24-31
normalized bonds :
11-12 11-16 12-13 13-14 14-15 15-16 25-26 25-30 26-27 27-28 28-29 29-30
isolated ring systems :
containing 1 : 11 : 25 :

G1:N,CH

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 8:CLASS 9:CLASS 10:CLASS 11:Atom
12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:CLASS 18:CLASS 19:CLASS 20:CLASS
21:Atom 23:CLASS 24:CLASS 25:Atom 26:Atom 27:Atom 28:Atom 29:Atom 30:Atom
31:CLASS 32:Atom 35:CLASS 36:Atom

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PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page for STN Seminar Schedule - N. America
NEWS 2	JUL 02	LMEDLINE coverage updated
NEWS 3	JUL 02	SCISEARCH enhanced with complete author names
NEWS 4	JUL 02	CHEMCATS accession numbers revised
NEWS 5	JUL 02	CA/CAplus enhanced with utility model patents from China
NEWS 6	JUL 16	CAplus enhanced with French and German abstracts
NEWS 7	JUL 18	CA/CAplus patent coverage enhanced
NEWS 8	JUL 26	USPATFULL/USPAT2 enhanced with IPC reclassification
NEWS 9	JUL 30	USGENE now available on STN
NEWS 10	AUG 06	CAS REGISTRY enhanced with new experimental property tags
NEWS 11	AUG 06	BEILSTEIN updated with new compounds
NEWS 12	AUG 06	FSTA enhanced with new thesaurus edition
NEWS 13	AUG 13	CA/CAplus enhanced with additional kind codes for granted patents
NEWS 14	AUG 20	CA/CAplus enhanced with CAS indexing in pre-1907 records
NEWS 15	AUG 27	Full-text patent databases enhanced with predefined patent family display formats from INPADOCDB
NEWS 16	AUG 27	USPATOLD now available on STN
NEWS 17	AUG 28	CAS REGISTRY enhanced with additional experimental spectral property data
NEWS 18	SEP 07	STN AnaVist, Version 2.0, now available with Derwent World Patents Index
NEWS 19	SEP 13	FORIS renamed to SOFIS
NEWS 20	SEP 13	INPADOCDB enhanced with monthly SDI frequency
NEWS 21	SEP 17	CA/CAplus enhanced with printed CA page images from 1967-1998
NEWS 22	SEP 17	CAplus coverage extended to include traditional medicine patents
NEWS 23	SEP 24	EMBASE, EMBAL, and LEMBASE reloaded with enhancements

NEWS EXPRESS 19 SEPTEMBER 2007: CURRENT WINDOWS VERSION IS V8.2, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 19 SEPTEMBER 2007.

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
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Updated Search

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* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 16:47:58 ON 01 OCT 2007

=> file reg
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 16:48:04 ON 01 OCT 2007
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 30 SEP 2007 HIGHEST RN 948879-65-0
DICTIONARY FILE UPDATES: 30 SEP 2007 HIGHEST RN 948879-65-0

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TSCA INFORMATION NOW CURRENT THROUGH June 29, 2007

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predicted properties as well as tags indicating availability of
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on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=> d his

(FILE 'HOME' ENTERED AT 16:47:58 ON 01 OCT 2007)

FILE 'REGISTRY' ENTERED AT 16:48:04 ON 01 OCT 2007

=>
Uploading C:\Documents and Settings\brobinson1\My
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L1 STRUCTURE UPLOADED

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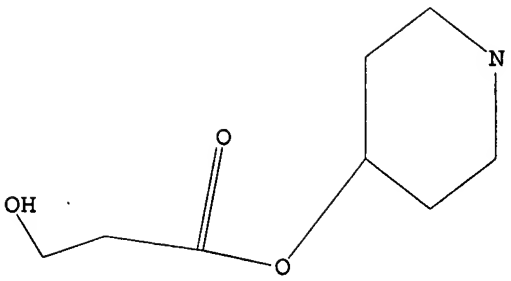
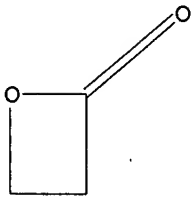
L1 HAS NO ANSWERS
L1 STR

Updated Search





Structure attributes must be viewed using STN Express query preparation.

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L2 STRUCTURE UPLOADED

=> d l2
L2 HAS NO ANSWERS
L2 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

=> s l2
SAMPLE SEARCH INITIATED 16:53:53 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 660 TO ITERATE

100.0% PROCESSED 660 ITERATIONS 8 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 11659 TO 14741
PROJECTED ANSWERS: 8 TO 329

L3 8 SEA SSS SAM L2

=> s l2 full
THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 171.65 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y

Updated Search

FULL SEARCH INITIATED 16:53:57 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 13471 TO ITERATE

100.0% PROCESSED 13471 ITERATIONS 207 ANSWERS
SEARCH TIME: 00.00.01

L4 207 SEA SSS FUL L2

=> file hcaplus
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 176.15 176.36

FILE 'HCAPLUS' ENTERED AT 16:54:00 ON 01 OCT 2007
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FILE COVERS 1907 - 1 Oct 2007 VOL 147 ISS 15
FILE LAST UPDATED: 30 Sep 2007 (20070930/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> s l4
L5 16 L4

=> s l5 and bold, g?/au
100 BOLD, G?/AU
L6 5 L5 AND BOLD, G?/AU

=> d l6, ibib abs hitstr, 1-5

L6 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:. 2004:515506 HCAPLUS
DOCUMENT NUMBER: 141:71453
TITLE: Preparation of anthranilic acid amide derivatives as neoplastic inhibitors
INVENTOR(S): Bold, Guido; Furet, Pascal; Manley, Paul William
PATENT ASSIGNEE(S): Novartis Ag, Switz.; Novartis Pharma GmbH
SOURCE: PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

Updated Search

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004052884	A1	20040624	WO 2003-EP14086		20031211
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RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR					
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AU 2003294834	A1	20040630	AU 2003-294834		20031211
EP 1572686	A1	20050914	EP 2003-785795		20031211
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BR 2003017292	A	20051108	BR 2003-17292		20031211
CN 1720244	A	20060111	CN 2003-80104845		20031211
JP 2006511518	T	20060406	JP 2004-558075		20031211
US 2006128684	A1	20060615	US 2005-538199		20050609
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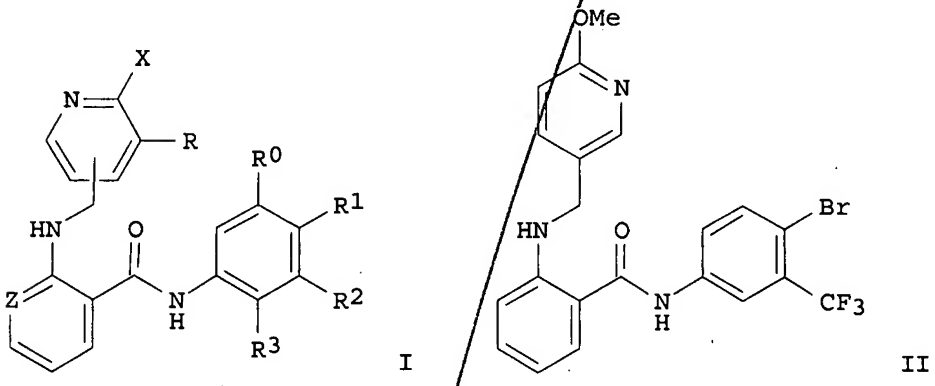
			WO 2003-EP14086	W	20031211

OTHER SOURCE(S): MARPAT 141:71453

GI



I II

AB The title compds. I [wherein R and R0 = independently H, halo, (un)substituted alkyl, alkenyl, alkynyl, aryl, heteroaryl, etc.; R1 = H, halo, (un)substituted alkyl, alkenyl, alkynyl, alkoxy, OCF3, OCH2CF3, OCH2CH2CF3, or OCH2CH2CH2CF3; R2 = perfluoroalkyl; R3 = H or halo; X = OH, alkoxy, alkylthio, imino, alkylimino, halo, etc.; Z = N or CH] or salts, N-oxides, or tautomers thereof are prepared as neoplastic inhibitors for the treatment of human or animal body. For example, the compound II was prepared in a multi-step synthesis. Formulations containing I as an active ingredient were also described.

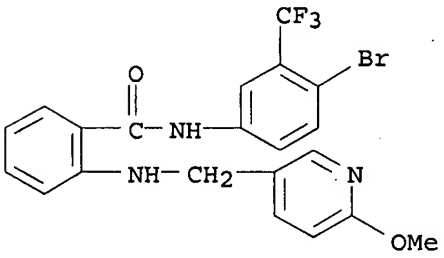
IT 524728-97-0P 524729-01-9P 657401-06-4P
709044-84-8P 709044-87-1P 709044-88-2P
709044-93-9P 709044-99-5P 709045-02-3P
709045-04-5P 709045-05-6P 709045-08-9P
709045-10-3P 709045-11-4P 709045-28-3P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate, reactant; preparation of anthranilic acid amide derivs. as

Updated Search

neoplastic inhibitors)

RN 524728-97-0 HCAPLUS

CN Benzamide, N-[4-bromo-3-(trifluoromethyl)phenyl]-2-[[(6-methoxy-3-pyridinyl)methyl]amino]- (9CI) (CA INDEX NAME)



RN 524729-01-9 HCAPLUS

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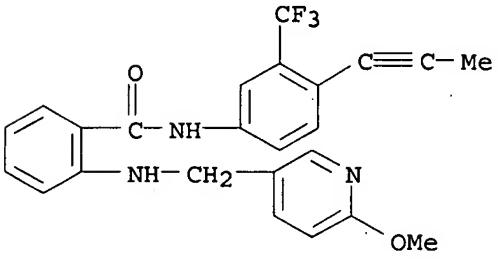

RN 657401-06-4 HCAPLUS

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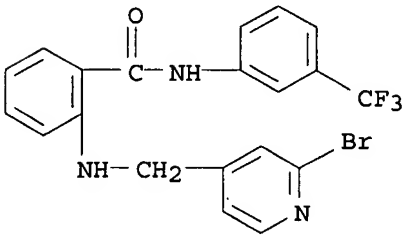
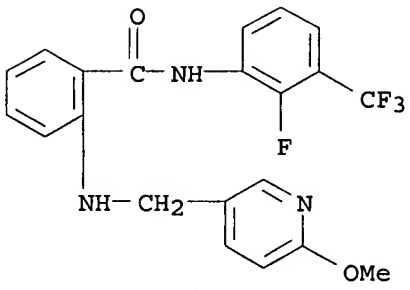


RN 709044-84-8 HCAPLUS

CN Benzamide, N-[2-fluoro-3-(trifluoromethyl)phenyl]-2-[[(6-methoxy-3-pyridinyl)methyl]amino]- (CA INDEX NAME)

Updated Search



RN 709044-87-1 HCAPLUS
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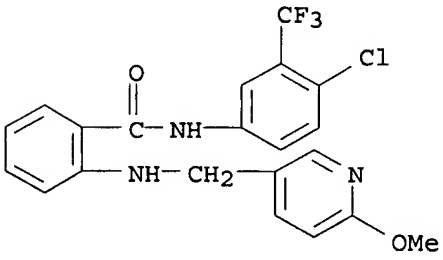

RN 709044-88-2 HCAPLUS
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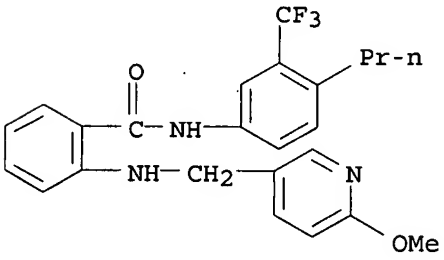
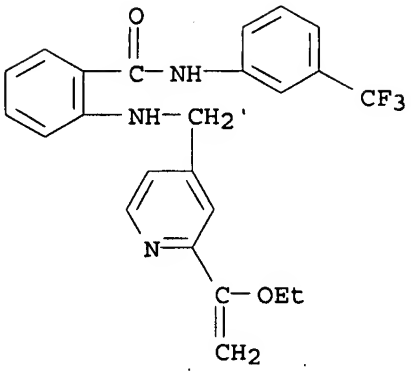


●x HCl

RN 709044-93-9 HCAPLUS
CN Benzamide, 2-[[[2-(1-ethoxyethenyl)-4-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

Updated Search



RN 709044-99-5 HCAPLUS
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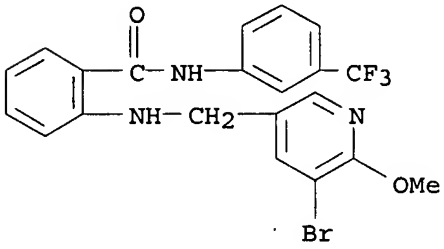

RN 709045-02-3 HCAPLUS
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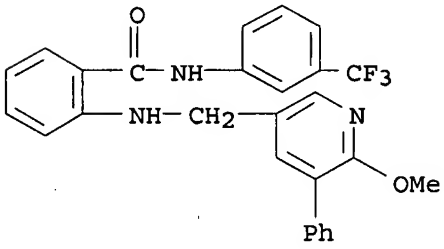

RN 709045-04-5 HCAPLUS
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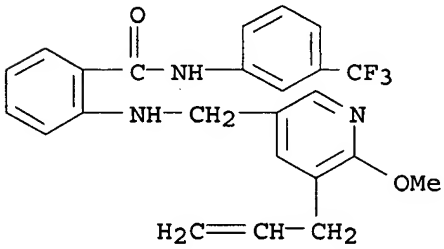

Updated Search

RN 709045-05-6 HCAPLUS
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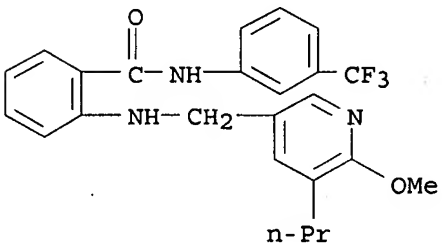
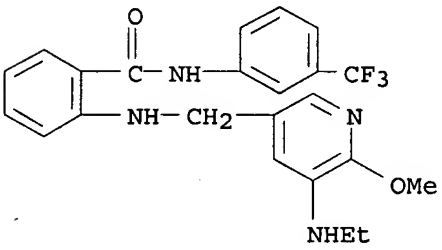


RN 709045-08-9 HCAPLUS
CN Benzamide, 2-[[[5-(ethylamino)-6-methoxy-3-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



RN 709045-10-3 HCAPLUS
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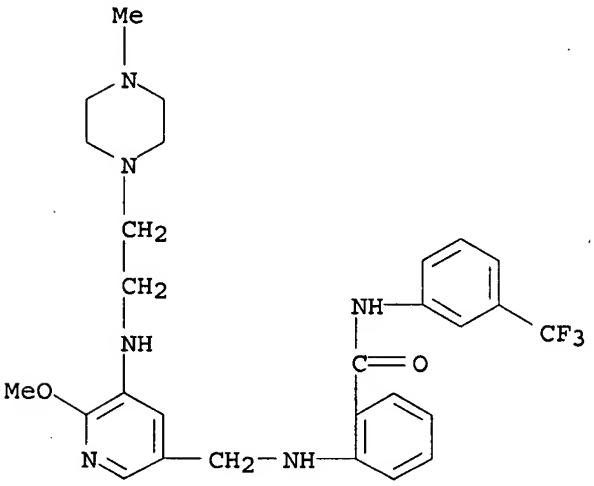
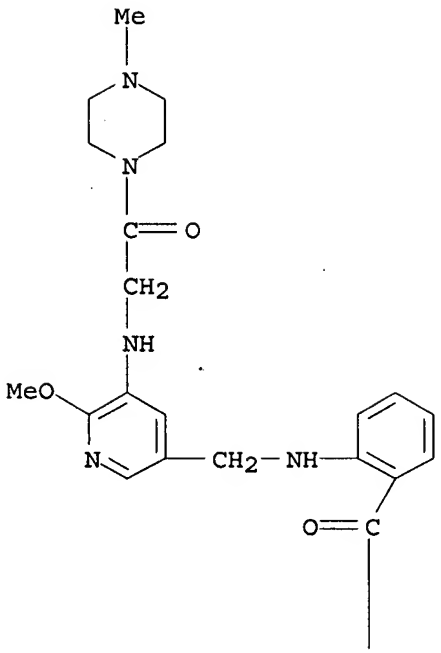


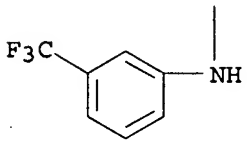
RN 709045-11-4 HCAPLUS
CN Benzamide, 2-[[[6-methoxy-5-[[2-(4-methyl-1-piperazinyl)-2-oxoethyl]amino]-3-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

Updated Search

PAGE 1-A



PAGE 2-A



RN 709045-28-3 HCAPLUS
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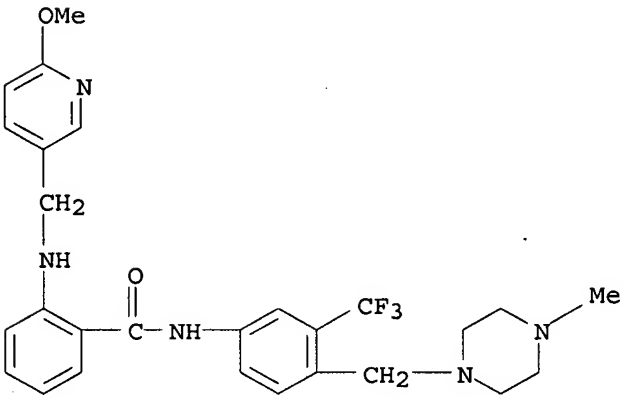

IT 709044-83-7P 709044-89-3P 709044-90-6P
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Updated Search

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709045-71-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of anthranilic acid amide derivs. as neoplastic inhibitors)

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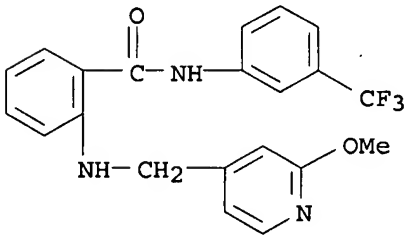
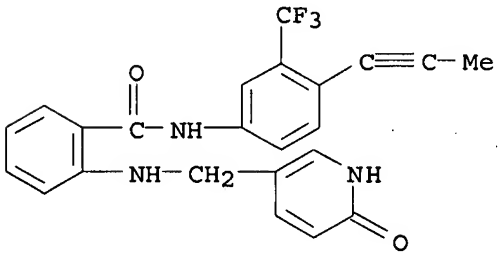
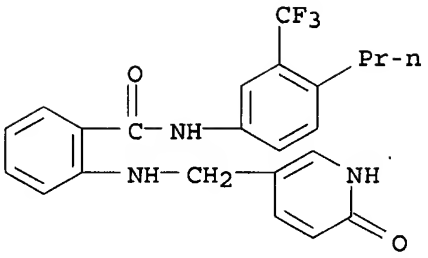


RN 709044-89-3 HCAPLUS
CN Benzamide, 2-[[(1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[4-(1-propynyl)-3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

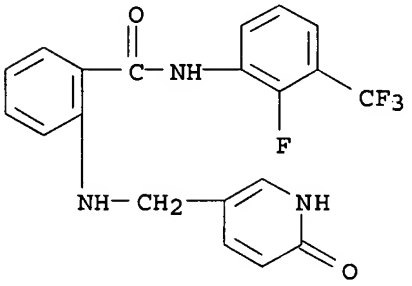


RN 709044-90-6 HCAPLUS
CN Benzamide, 2-[[(1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[4-propyl-3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

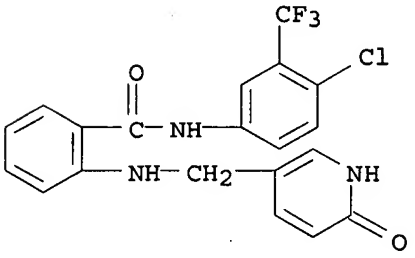
Updated Search



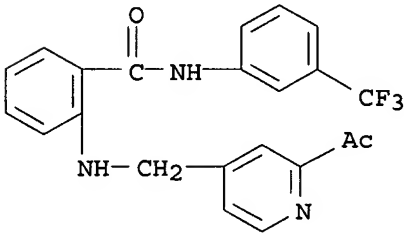
RN 709044-91-7 HCAPLUS
CN Benzamide, 2-[[(1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[2-fluoro-3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



RN 709044-92-8 HCAPLUS
CN Benzamide, N-[4-chloro-3-(trifluoromethyl)phenyl]-2-[[(1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]- (CA INDEX NAME)



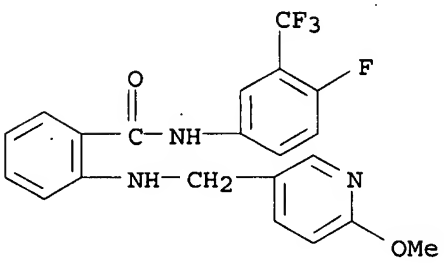
RN 709044-94-0 HCAPLUS
CN Benzamide, 2-[[(2-acetyl-4-pyridinyl)methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



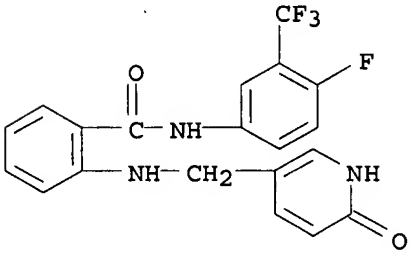
RN 709044-95-1 HCAPLUS

Updated Search

CN Benzamide, N-[4-fluoro-3-(trifluoromethyl)phenyl]-2-[[(6-methoxy-3-pyridinyl)methyl]amino]- (CA INDEX NAME)



RN 709044-97-3 HCAPLUS
CN Benzamide, 2-[[(1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[4-fluoro-3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



RN 709045-01-2 HCAPLUS
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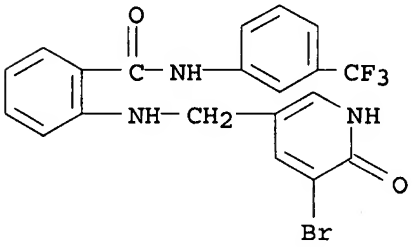
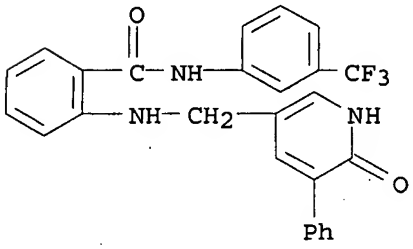
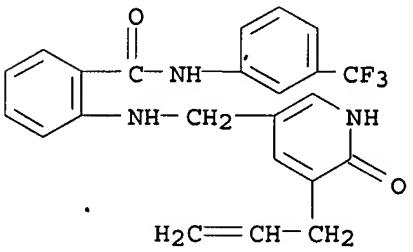


RN 709045-03-4 HCAPLUS
CN Benzamide, 2-[[(1,6-dihydro-6-oxo-5-phenyl-3-pyridinyl)methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

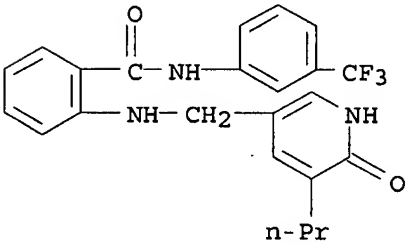


Updated Search

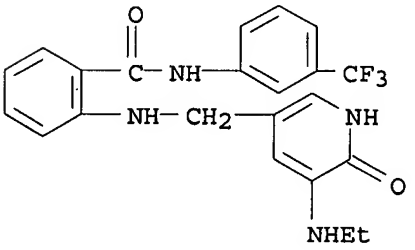
RN 709045-06-7 HCAPLUS
CN Benzamide, 2-[[[1,6-dihydro-6-oxo-5-(2-propenyl)-3-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 709045-07-8 HCAPLUS
CN Benzamide, 2-[[(1,6-dihydro-6-oxo-5-propyl-3-pyridinyl)methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



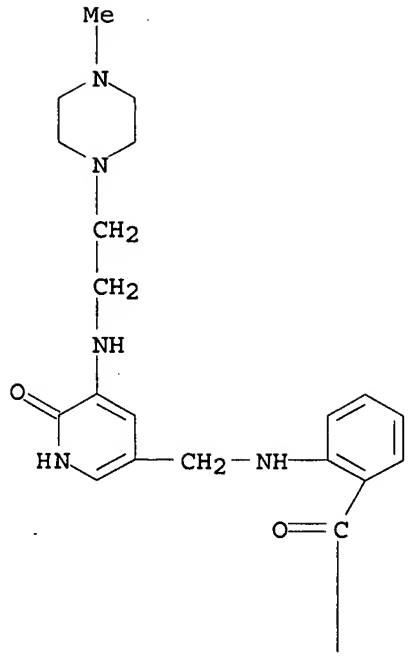
RN 709045-09-0 HCAPLUS
CN Benzamide, 2-[[[5-(ethylamino)-1,6-dihydro-6-oxo-3-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



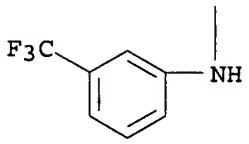
RN 709045-12-5 HCAPLUS
CN Benzamide, 2-[[[1,6-dihydro-5-[[2-(4-methyl-1-piperazinyl)ethyl]amino]-6-oxo-3-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

Updated Search

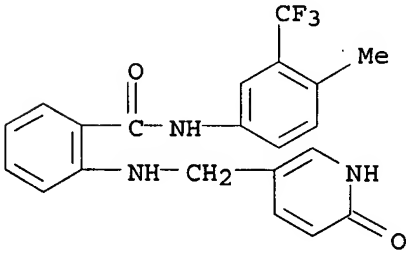
PAGE 1-A



PAGE 2-A

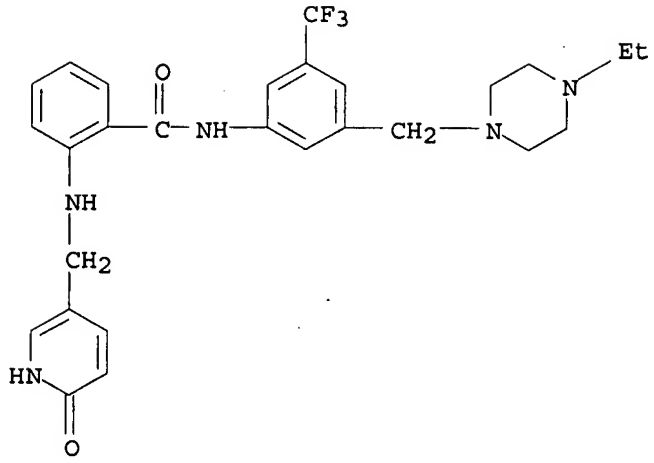


RN 709045-13-6 HCAPLUS
CN Benzamide, 2-[[(1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[4-methyl-3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

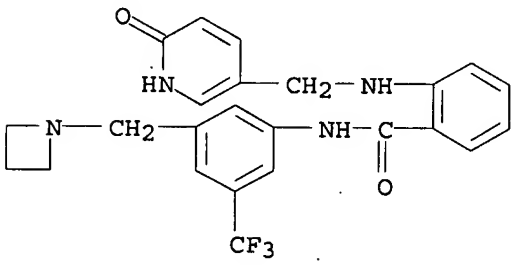


RN 709045-17-0 HCAPLUS
CN Benzamide, 2-[[(1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[3-[(4-ethyl-1-piperazinyl)methyl]-5-(trifluoromethyl)phenyl]- (CA INDEX NAME)

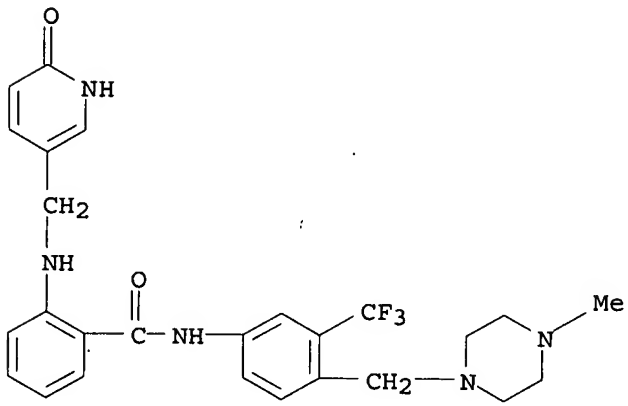
Updated Search



RN 709045-21-6 HCAPLUS
CN Benzamide, N-[3-(1-azetidinylmethyl)-5-(trifluoromethyl)phenyl]-2-[[(1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]- (CA INDEX NAME)

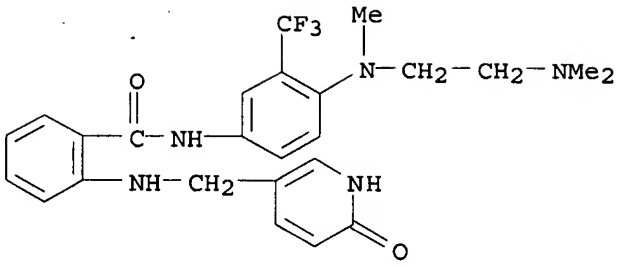


RN 709045-32-9 HCAPLUS
CN Benzamide, 2-[[(1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[4-[(4-methyl-1-piperazinyl)methyl]-3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

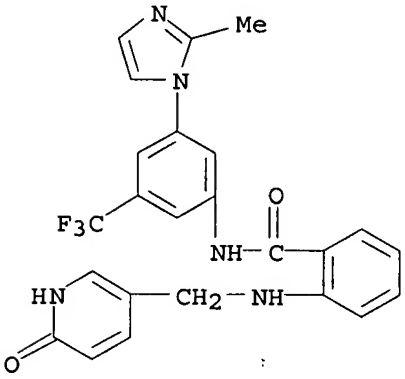


RN 709045-33-0 HCAPLUS
CN Benzamide, 2-[[(1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[4-[[2-(dimethylamino)ethyl]methylamino]-3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

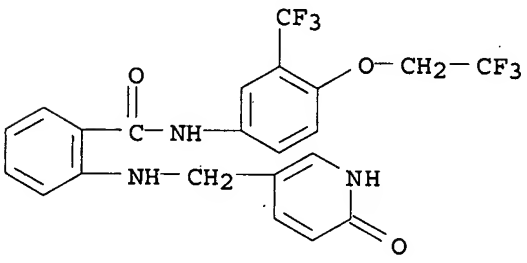
Updated Search



RN 709045-34-1 HCAPLUS
CN Benzamide, 2-[[(1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[3-(2-methyl-1H-imidazol-1-yl)-5-(trifluoromethyl)phenyl]- (CA INDEX NAME)

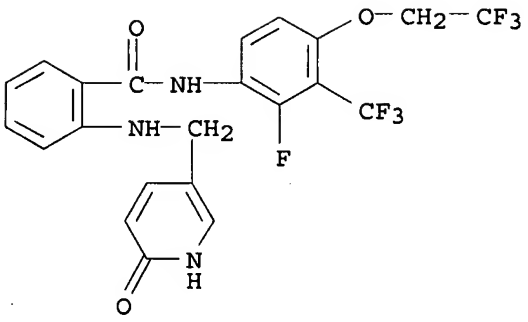


RN 709045-37-4 HCAPLUS
CN Benzamide, 2-[[(1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[4-(2,2,2-trifluoroethoxy)-3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

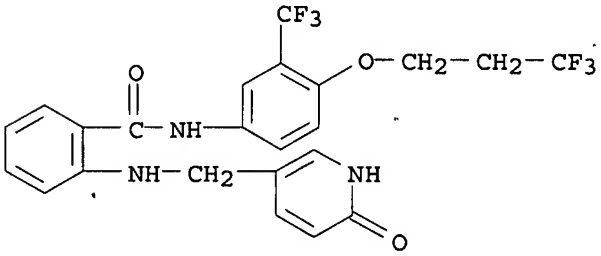


RN 709045-38-5 HCAPLUS
CN Benzamide, 2-[[(1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[2-fluoro-4-(2,2,2-trifluoroethoxy)-3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

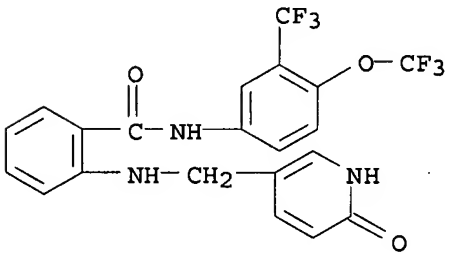
Updated Search



RN 709045-39-6 HCAPLUS
CN Benzamide, 2-[[(1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[3-(trifluoromethyl)-4-(3,3,3-trifluoropropoxy)phenyl]- (CA INDEX NAME)

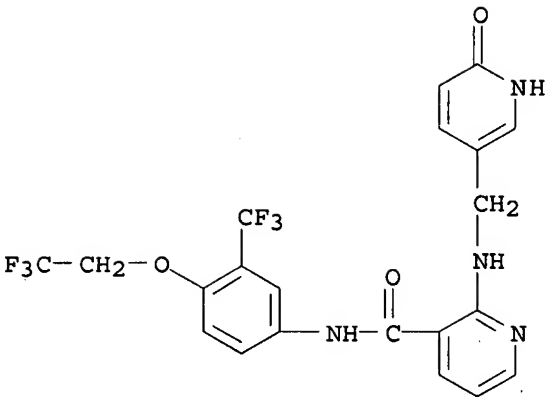


RN 709045-40-9 HCAPLUS
CN Benzamide, 2-[[(1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[4-(trifluoromethoxy)-3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

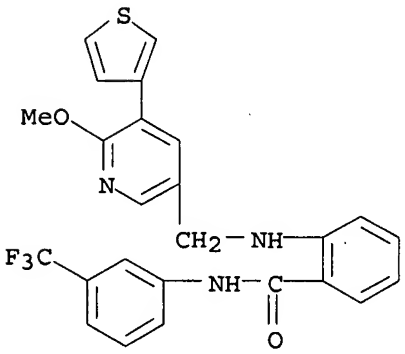


RN 709045-41-0 HCAPLUS
CN 3-Pyridinecarboxamide, 2-[[(1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[4-(2,2,2-trifluoroethoxy)-3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

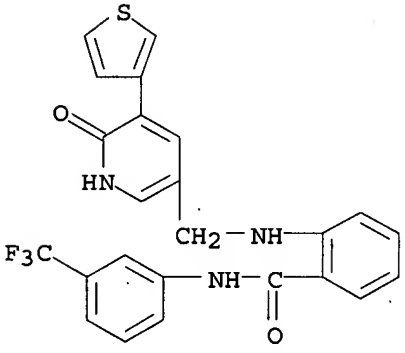
Updated Search



RN 709045-42-1 HCAPLUS
CN Benzamide, 2-[[[6-methoxy-5-(3-thienyl)-3-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

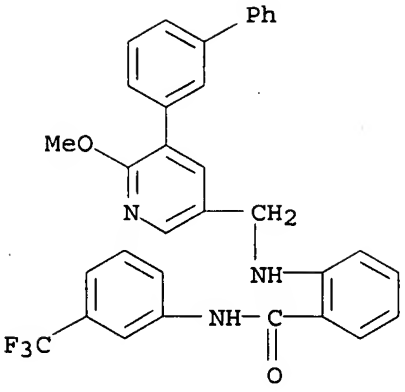


RN 709045-43-2 HCAPLUS
CN Benzamide, 2-[[[1,6-dihydro-6-oxo-5-(3-thienyl)-3-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

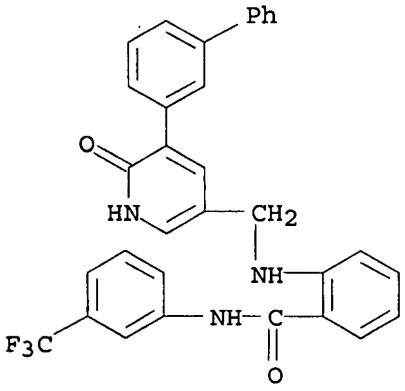


RN 709045-44-3 HCAPLUS
CN Benzamide, 2-[[(5-[1,1'-biphenyl]-3-yl-6-methoxy-3-pyridinyl)methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

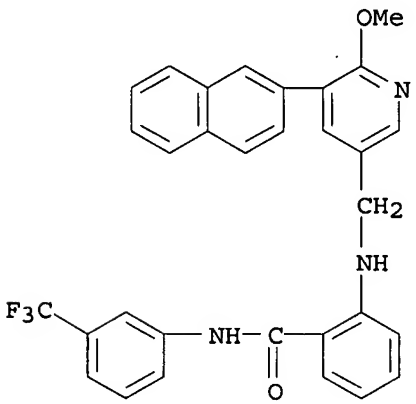
Updated Search



RN 709045-45-4 HCAPLUS
CN Benzamide, 2-[[(5-[1,1'-biphenyl]-3-yl-1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

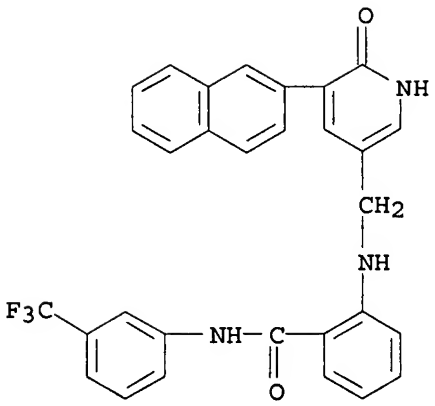


RN 709045-46-5 HCAPLUS
CN Benzamide, 2-[[[6-methoxy-5-(2-naphthalenyl)-3-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

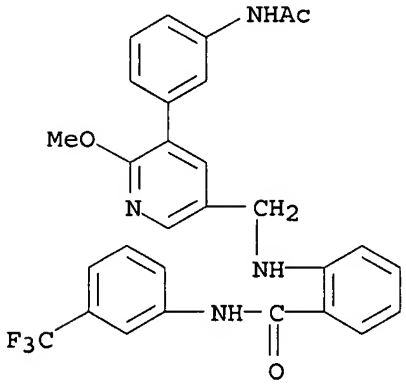


RN 709045-47-6 HCAPLUS
CN Benzamide, 2-[[[1,6-dihydro-5-(2-naphthalenyl)-6-oxo-3-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

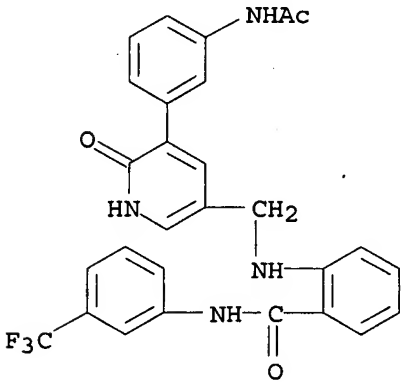
Updated Search



RN 709045-48-7 HCAPLUS
CN Benzamide, 2-[[[5-[3-(acetylamino)phenyl]-6-methoxy-3-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



RN 709045-49-8 HCAPLUS
CN Benzamide, 2-[[[5-[3-(acetylamino)phenyl]-1,6-dihydro-6-oxo-3-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



RN 709045-50-1 HCAPLUS

Updated Search

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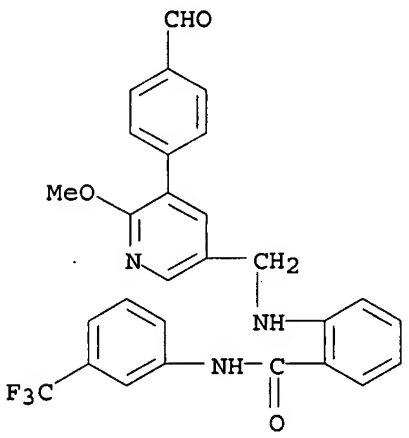
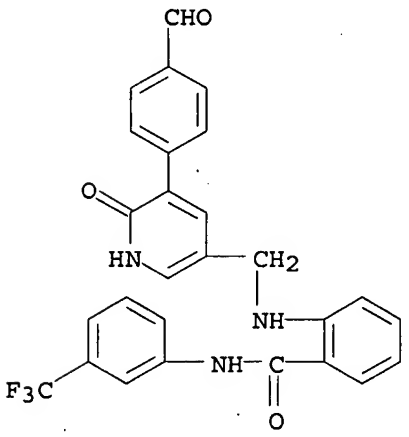
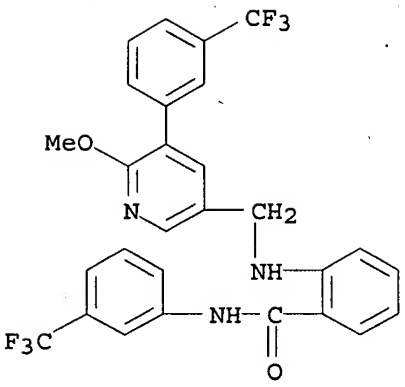


RN 709045-51-2 HCAPLUS
CN Benzamide, 2-[[[5-(4-formylphenyl)-1,6-dihydro-6-oxo-3-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

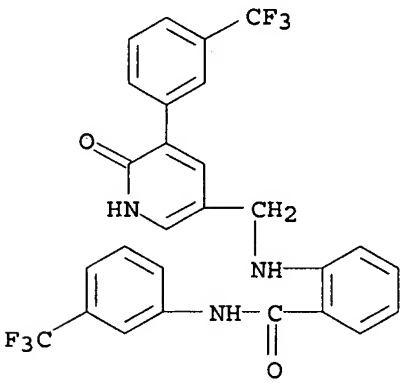


RN 709045-52-3 HCAPLUS
CN Benzamide, 2-[[[6-methoxy-5-[3-(trifluoromethyl)phenyl]-3-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

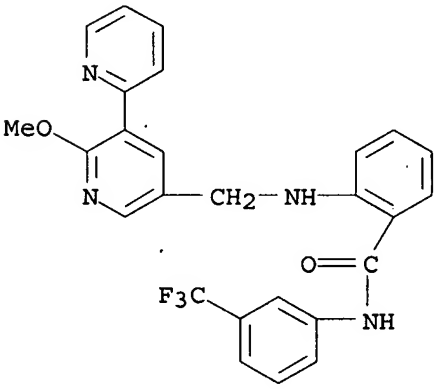
Updated Search



RN 709045-53-4 HCAPLUS
CN Benzamide, 2-[[[1,6-dihydro-6-oxo-5-[3-(trifluoromethyl)phenyl]-3-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



RN 709045-54-5 HCAPLUS
CN Benzamide, 2-[[(2'-methoxy[2,3'-bipyridin]-5'-yl)methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



RN 709045-55-6 HCAPLUS
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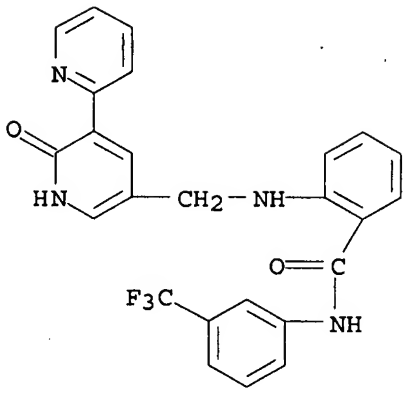
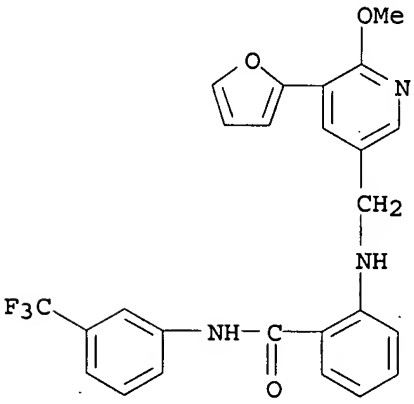
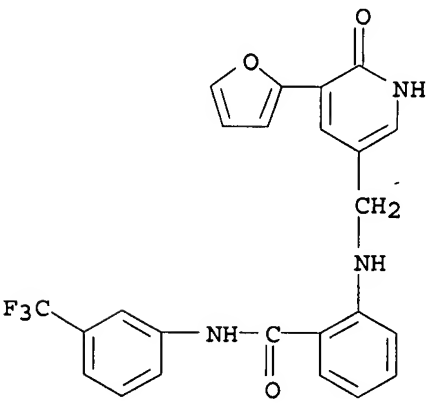
Updated Search



RN 709045-56-7 HCAPLUS
CN Benzamide, 2-[[[5-(2-furanyl)-6-methoxy-3-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



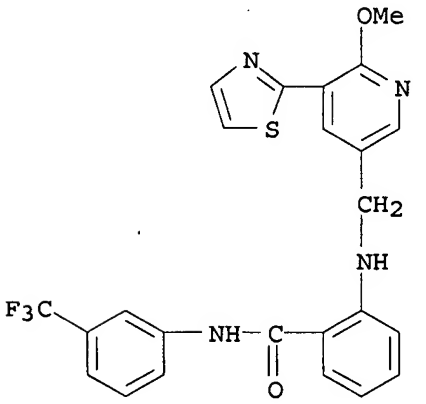
RN 709045-57-8 HCAPLUS
CN Benzamide, 2-[[[5-(2-furanyl)-1,6-dihydro-6-oxo-3-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



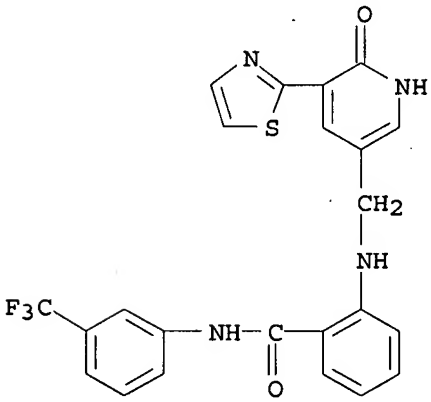
RN 709045-58-9 HCAPLUS

Updated Search

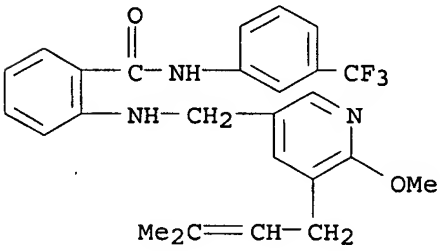
CN Benzamide, 2-[[[6-methoxy-5-(2-thiazolyl)-3-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



RN 709045-59-0 HCAPLUS
CN Benzamide, 2-[[[1,6-dihydro-6-oxo-5-(2-thiazolyl)-3-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

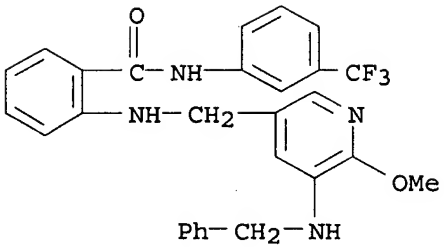


RN 709045-60-3 HCAPLUS
CN Benzamide, 2-[[[6-methoxy-5-(3-methyl-2-butenyl)-3-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

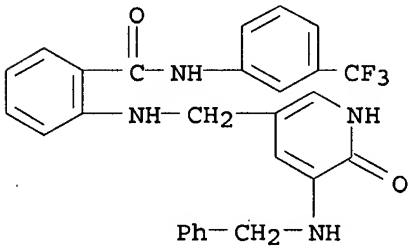


RN 709045-61-4 HCAPLUS
CN Benzamide, 2-[[[6-methoxy-5-[(phenylmethyl)amino]-3-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

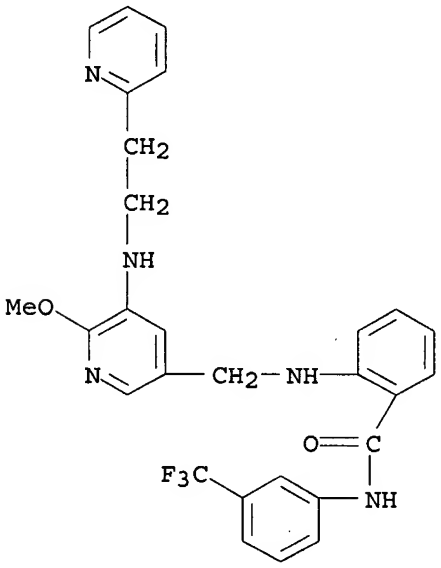
Updated Search



RN 709045-62-5 HCAPLUS
CN Benzamide, 2-[[[1,6-dihydro-6-oxo-5-[(phenylmethyl)amino]-3-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

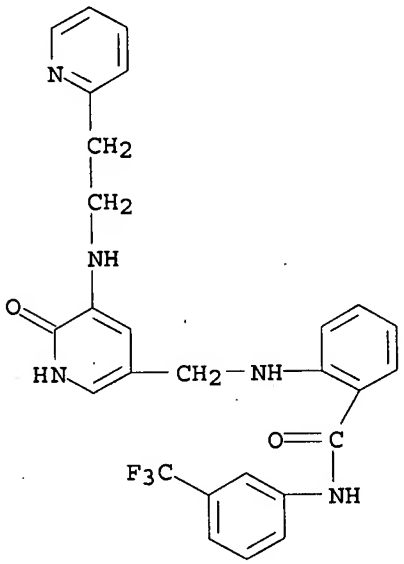


RN 709045-63-6 HCAPLUS
CN Benzamide, 2-[[[6-methoxy-5-[[2-(2-pyridinyl)ethyl]amino]-3-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

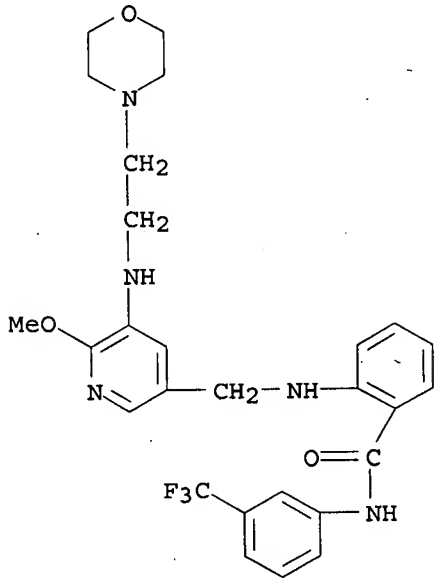


RN 709045-64-7 HCAPLUS
CN Benzamide, 2-[[[1,6-dihydro-6-oxo-5-[[2-(2-pyridinyl)ethyl]amino]-3-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

Updated Search

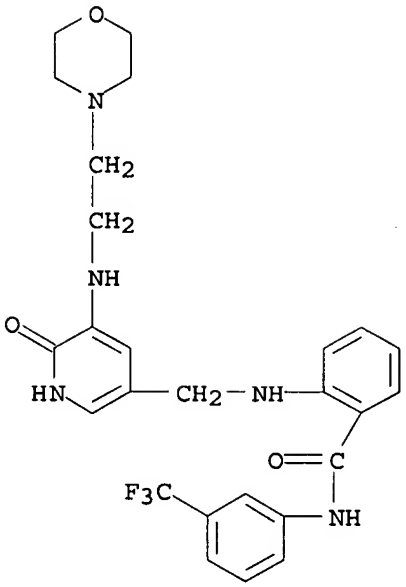


RN 709045-65-8 HCAPLUS
CN Benzamide, 2-[[[6-methoxy-5-[[2-(4-morpholinyl)ethyl]amino]-3-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

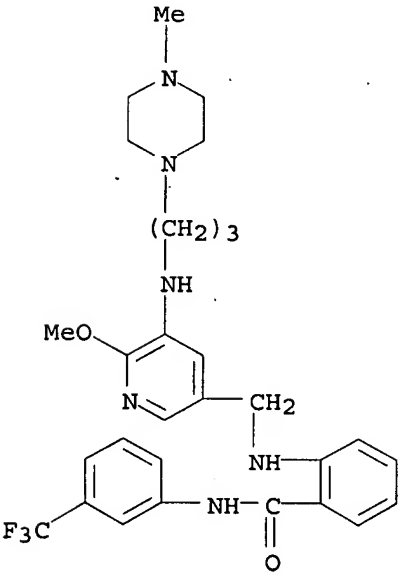


RN 709045-66-9 HCAPLUS
CN Benzamide, 2-[[[1,6-dihydro-5-[[2-(4-morpholinyl)ethyl]amino]-6-oxo-3-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

Updated Search

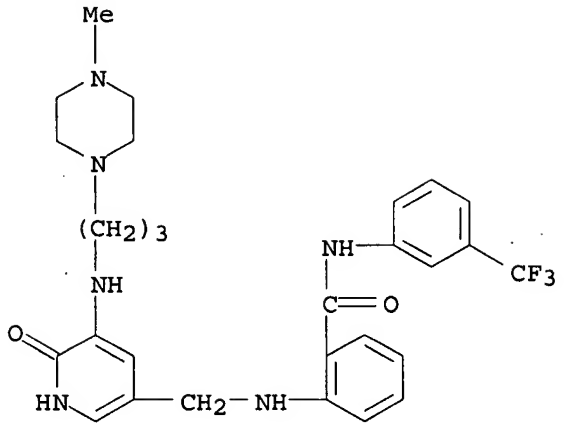


RN 709045-67-0 HCAPLUS
CN Benzamide, 2-[[[6-methoxy-5-[[3-(4-methyl-1-piperazinyl)propyl]amino]-3-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



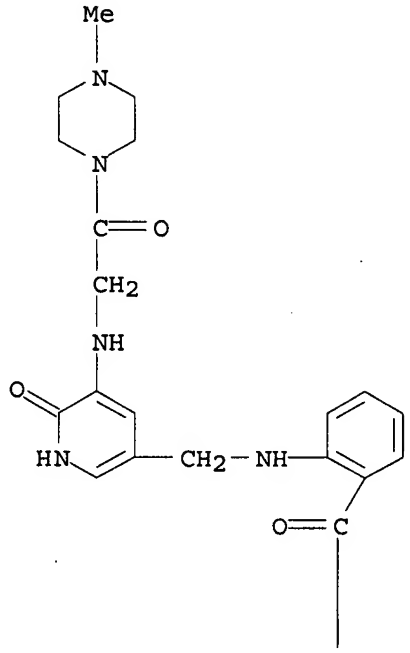
RN 709045-68-1 HCAPLUS
CN Benzamide, 2-[[[1,6-dihydro-5-[[3-(4-methyl-1-piperazinyl)propyl]amino]-6-oxo-3-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

Updated Search

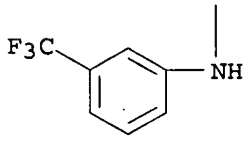


RN 709045-69-2 HCAPLUS
CN Benzamide, 2-[[[1,6-dihydro-5-[[2-(4-methyl-1-piperazinyl)-2-oxoethyl]amino]-6-oxo-3-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

PAGE 1-A

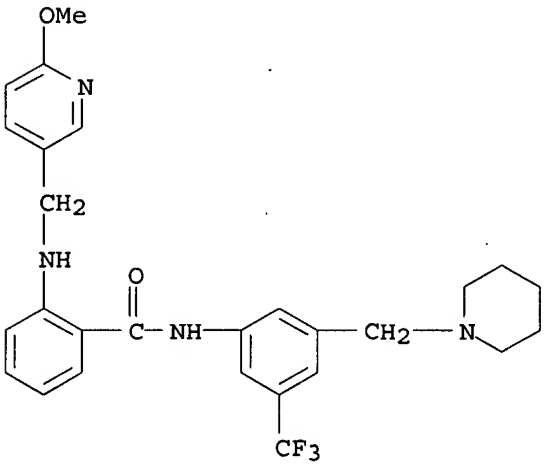


PAGE 2-A

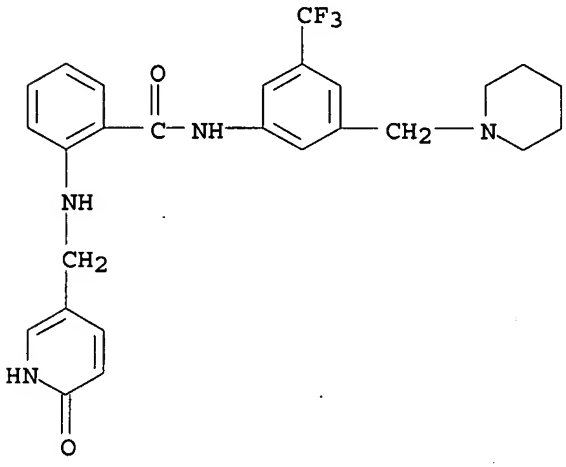


Updated Search

RN 709045-70-5 HCAPLUS
CN Benzamide, 2-[[(6-methoxy-3-pyridinyl)methyl]amino]-N-[3-(1-piperidinylmethyl)-5-(trifluoromethyl)phenyl]- (CA INDEX NAME)

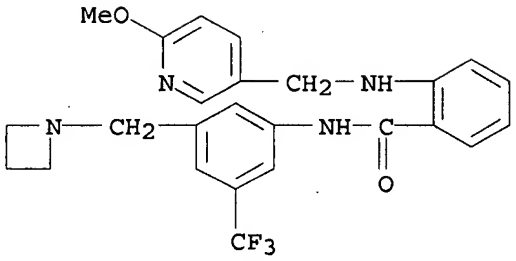


RN 709045-71-6 HCAPLUS
CN Benzamide, 2-[[(1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[3-(1-piperidinylmethyl)-5-(trifluoromethyl)phenyl]- (CA INDEX NAME)



IT 709045-22-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of anthranilic acid amide derivs. as neoplastic inhibitors)
RN 709045-22-7 HCAPLUS
CN Benzamide, N-[3-(1-azetidinylmethyl)-5-(trifluoromethyl)phenyl]-2-[[(6-methoxy-3-pyridinyl)methyl]amino]- (CA INDEX NAME)

Updated Search



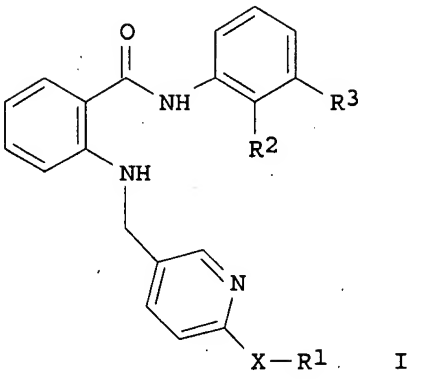
L6 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:376825 HCAPLUS
DOCUMENT NUMBER: 138:385308
TITLE: Preparation of anthranilic acid amides and their use as vascular endothelial growth factor receptor tyrosine kinase inhibitors
INVENTOR(S): Bold, Guido; Furet, Pascal; Manley, Paul William
PATENT ASSIGNEE(S): Novartis AG, Switz.; Novartis Pharma Gmbh
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003040102	A1	20030515	WO 2002-EP12444	20021107
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NO, NZ, OM, PH, PL, PT, RO, RU, SE, SG, SI, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR				
TW 260222	B	20060821	TW 2002-91132669	20021106
CA 2463968	A1	20030515	CA 2002-2463968	20021107
AU 2002351909	A1	20030519	AU 2002-351909	20021107
AU 2002351909	B2	20070426		
EP 1446382	A1	20040818	EP 2002-787595	20021107
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
BR 2002013970	A	20040831	BR 2002-13970	20021107
CN 1585750	A	20050223	CN 2002-822209	20021107
JP 2005511602	T	20050428	JP 2003-542148	20021107
NZ 532590	A	20051223	NZ 2002-532590	20021107
ZA 2004002940	A	20050210	ZA 2004-2940	20040419
US 2005096356	A1	20050505	US 2004-494591	20040505
US 7091224	B2	20060815		
IN 2004CN00972	A	20060203	IN 2004-CN972	20040506
NO 2004002187	A	20040526	NO 2004-2187	20040526
US 2006178409	A1	20060810	US 2006-374720	20060314

PRIORITY APPLN. INFO.:
GB 2001-26902 A 20011108
WO 2002-EP12444 W 20021107
US 2004-494591 A1 20040505

OTHER SOURCE(S): MARPAT 138:385308
GI

Updated Search



I

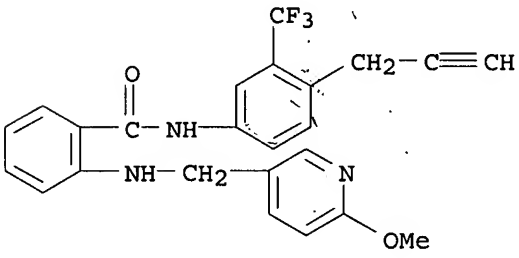
1034

AB Anthranilic acid amide derivs. [I; R1, R2 = H, lower alkyl; R3 = lower perfluoroalkyl; X = O, S; e.g., 2-[(6-Methoxy-3-pyridinyl)methyl]amino-N-[3-(trifluoromethyl)phenyl]benzamide hydrochloride, m.p. 133-135°], which are vascular endothelial growth factor receptor tyrosine kinase inhibitors for the treatment of neoplastic disease, of retinopathy or age-related macular degeneration, are prepared and a I-containing formulation presented (e.g., a soft capsule).

IT 524941-34-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(in the preparation of anthranilic acid amides)

RN 524941-34-2 HCAPLUS

CN Benzamide, 2-[[(6-methoxy-3-pyridinyl)methyl]amino]-N-[4-(2-propynyl)-3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

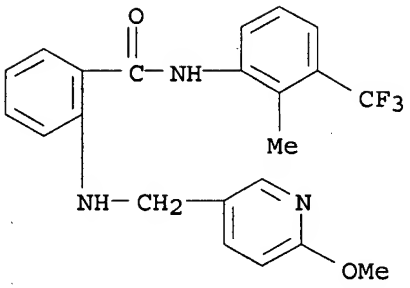


IT 524941-29-5P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(in the preparation of anthranilic acid amides for use as vascular endothelial growth factor receptor tyrosine kinase inhibitors)

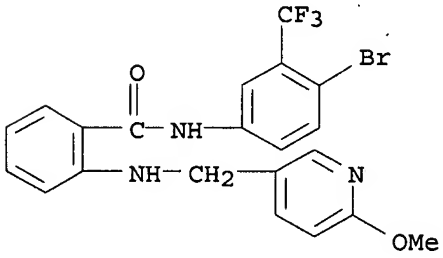
RN 524941-29-5 HCAPLUS

CN Benzamide, 2-[[(6-methoxy-3-pyridinyl)methyl]amino]-N-[2-methyl-3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

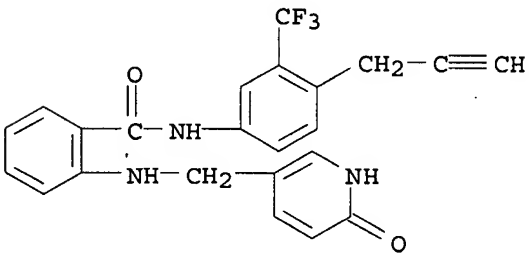
Updated Search



IT 524728-97-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of)
RN 524728-97-0 HCAPLUS
CN Benzamide, N-[4-bromo-3-(trifluoromethyl)phenyl]-2-[[(6-methoxy-3-pyridinyl)methyl]amino]- (9CI) (CA INDEX NAME)

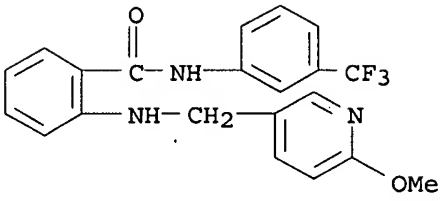


IT 524941-33-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 524941-33-1 HCAPLUS
CN Benzamide, 2-[[(1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[4-(2-propynyl)-3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



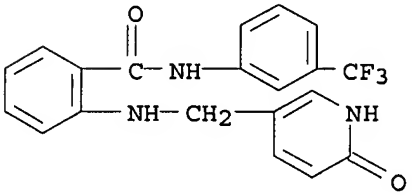
IT 524941-28-4P
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of anthranilic acid amides and their use as vascular endothelial growth factor receptor tyrosine kinase inhibitors)
RN 524941-28-4 HCAPLUS
CN Benzamide, 2-[[(6-methoxy-3-pyridinyl)methyl]amino]-N-[3-(trifluoromethyl)phenyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Updated Search

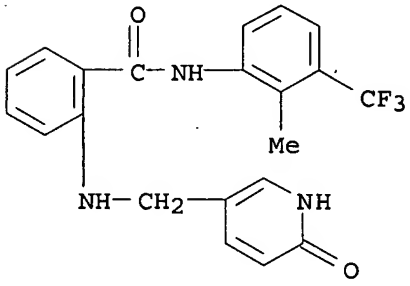


● HCl

IT 524941-35-3P 524941-36-4P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of anthranilic acid amides and their use as vascular endothelial growth factor receptor tyrosine kinase inhibitors)
RN 524941-35-3 HCAPLUS
CN Benzamide, 2-[[(1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 524941-36-4 HCAPLUS
CN Benzamide, 2-[[(1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[2-methyl-3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:376824 HCAPLUS
DOCUMENT NUMBER: 138:368777
TITLE: Preparation of pyridyl-substituted anthranilic acid amides for treating neoplastic disease
INVENTOR(S): Bold, Guido; Furet, Pascal; Manley, Paul William
PATENT ASSIGNEE(S): Novartis AG, Switz.; Novartis Pharma Gmbh

Updated Search

SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003040101	A1	20030515	WO 2002-EP12445	20021107
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SE, SG, SI, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR				
TW 260985	B	20060901	TW 2002-91132668	20021106
CA 2462390	A1	20030515	CA 2002-2462390	20021107
AU 2002342889	A1	20030519	AU 2002-342889	20021107
AU 2002342889	B2	20070301		
EP 1446381	A1	20040818	EP 2002-779536	20021107
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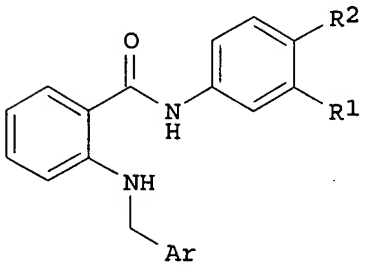
BR 2002013939	A	20040831	BR 2002-13939	20021107
CN 1578768	A	20050209	CN 2002-821430	20021107
JP 2005508382	T	20050331	JP 2003-542147	20021107
NZ 532587	A	20060224	NZ 2002-532587	20021107
NZ 543915	A	20070629	NZ 2002-543915	20021107
US 2004248947	A1	20041209	US 2004-494222	20040503
US 7067543	B2	20060627		
IN 2004CN00973	A	20060203	IN 2004-CN973	20040506
MX 2004PA04390	A	20050516	MX 2004-PA4390	20040507
NO 2004002137	A	20040525	NO 2004-2137	20040525
ZA 200402623	A	20060531	ZA 2004-2623	20060328

PRIORITY APPLN. INFO.:

GB 2001-26901	A	20011108
GB 2002-12917	A	20020605
NZ 2002-532587	A3	20021107
WO 2002-EP12445	W	20021107

OTHER SOURCE(S): MARPAT 138:368777
GI



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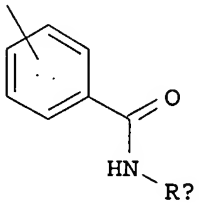


II

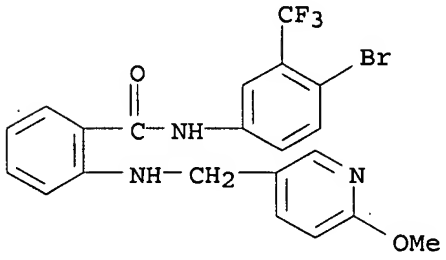
AB The title compds. [I; Ar = II (wherein Ra = H, alkyl; and R1 = H, perfluoroalkyl; R2 = H, halo, alkyl, alkenyl, alkynyl); or Ar = 4-pyridyl and R1 = perfluoroalkyl; R2 = Br, I, alkyl, alkenyl, alkynyl; or R1 = H, and R2 = F, Br, I, Et, alkyl, alkenyl or alkynyl] and their N-oxides and salts, useful for the treatment especially of a neoplastic disease, such as a

Updated Search

tumor disease, of retinopathy or age-related macular degeneration in the human or animal body, were prepared and formulated. Thus, reductive amination of 4-pyridinecarboxaldehyde with 2-amino-N-(4-bromo-3-trifluoromethylphenyl)benzamide (preparation given) in the presence of NaBH3CN afforded I [Ar = 4-pyridyl; R1 = CF3; R2 = Br]. The IC50-values that can be found for the compds. I are in range of 0.001 to 1 μM in test for activity against VEGF-receptor tyrosine kinase.

IT 524728-97-0P 524729-01-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of pyridyl-substituted anthranilic acid amides for treating neoplastic disease)

RN 524728-97-0 HCAPLUS
CN Benzamide, N-[4-bromo-3-(trifluoromethyl)phenyl]-2-[[(6-methoxy-3-pyridinyl)methyl]amino]- (9CI) (CA INDEX NAME)



RN 524729-01-9 HCAPLUS
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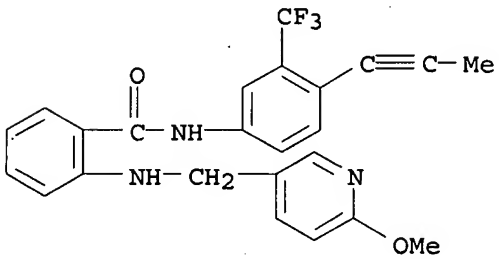

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:565010 HCAPLUS
DOCUMENT NUMBER: 135:137407
TITLE: Preparation of 2-aminonicotinamides as VEGF-receptor tyrosine kinase inhibitors
INVENTOR(S): Manley, Paul William; Bold, Guido
PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis-Erfindungen Verwaltungsgesellschaft m.b.H.
SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

Updated Search

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2001055114	A1	20010802	WO 2001-EP835		20010125
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
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AU 200128499	A	20010807	AU 2001-28499		20010125
AU 771626	B2	20040401			
BR 2001007805	A	20021022	BR 2001-7805		20010125
EP 1259487	A1	20021127	EP 2001-946854		20010125
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HU 200204083	A2	20030328	HU 2002-4083		20010125
JP 2003520853	T	20030708	JP 2001-555056		20010125
JP 3894793	B2	20070322			
NZ 520005	A	20040227	NZ 2001-520005		20010125
RU 2296124	C2	20070327	RU 2002-121645		20010125
NO 2002003218	A	20020916	NO 2002-3218		20020702
NO 323826	B1	20070709			
US 2003032656	A1	20030213	US 2002-181005		20020711
US 6624174	B2	20030923			
MX 2002PA07319	A	20021129	MX 2002-PA7319		20020726
ZA 2002005988	A	20030728	ZA 2002-5988		20020726
HK 1050895	A1	20051230	HK 2003-103030		20030429
PRIORITY APPLN. INFO.:			GB 2000-1930	A	20000127
			WO 2001-EP835	W	20010125

OTHER SOURCE(S): MARPAT 135:137407

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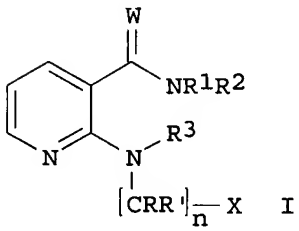

I

AB The title compds. [I; n = 1-6; W = O, S; R1, R3 = H, alkyl, acyl; R2 = (un)substituted cycloalkyl, aryl, mono- or bicyclic heteroaryl comprising one or more ring N atoms and 0-2 heteroatoms selected from O and S; R, R' = H, alkyl; X = (un)substituted aryl, mono- or bicyclic heteroaryl comprising one or more ring N atoms and 0-2 heteroatoms selected from O and S] and their pharmaceutically acceptable salts, useful for therapy of a disease which responds to an inhibition of the VEGF-receptor tyrosine kinase activity (such as neoplastic disease), were prepared and formulated. Thus, amidation of 3-aminobenzotrifluoride with 2-chloronicotinoyl chloride followed by reacting 4-pyridineethanamine with the resulting carboxamide afforded I [n = 2; R, R' = H; X = 4-pyridyl; W = O; R1, R3 = H; R2 = 3-(F3C)C6H4].

Updated Search

IT 352227-59-9P 352227-60-2P 352227-82-8P
352227-83-9P 352227-84-0P 352227-88-4P
352227-93-1P 352227-97-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 2-aminonicotinamides as VEGF-receptor tyrosine kinase inhibitors)

RN 352227-59-9 HCAPLUS
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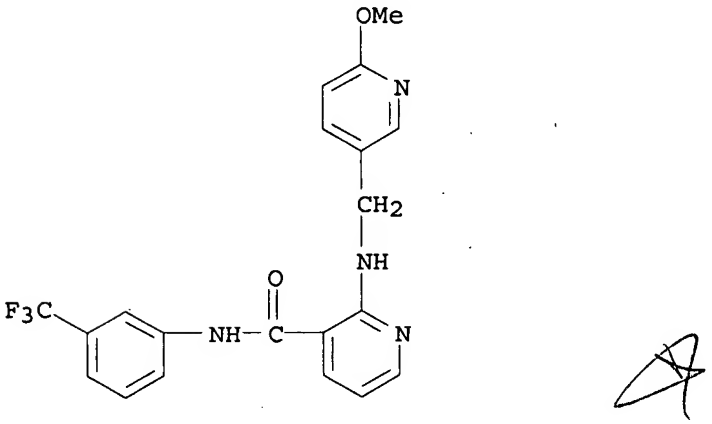

RN 352227-60-2 HCAPLUS
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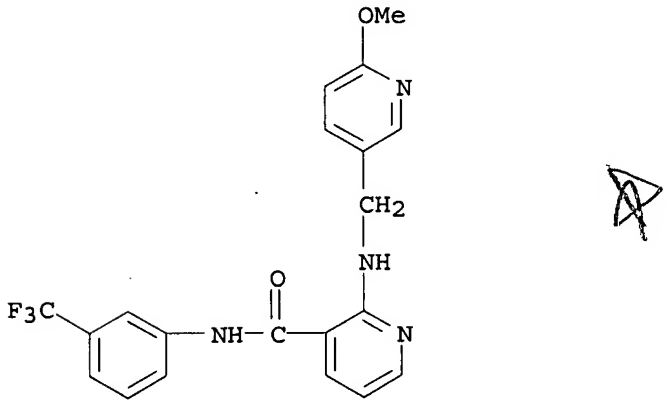

●2 HCl

RN 352227-82-8 HCAPLUS
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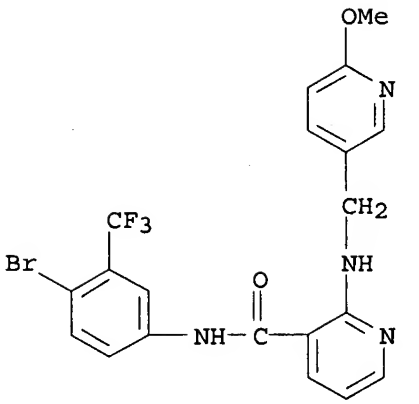
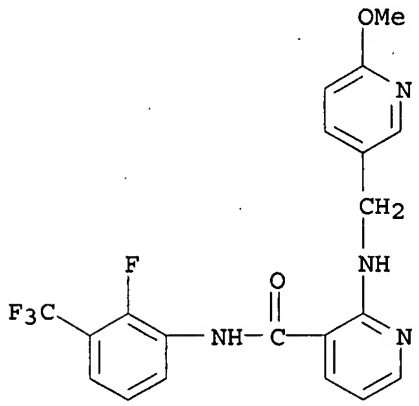
Updated Search



RN 352227-83-9 HCAPLUS
CN 3-Pyridinecarboxamide, N-[2-fluoro-3-(trifluoromethyl)phenyl]-2-[[(6-methoxy-3-pyridinyl)methyl]amino]- (9CI) (CA INDEX NAME)



RN 352227-84-0 HCAPLUS
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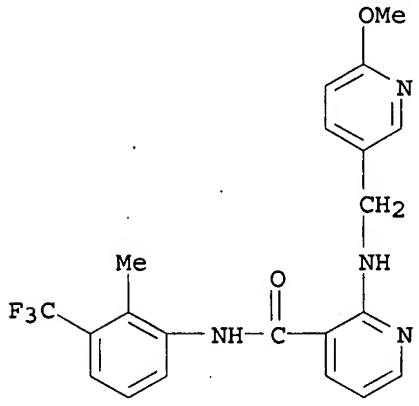
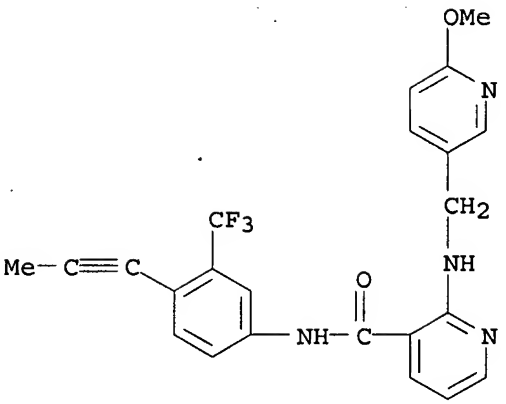
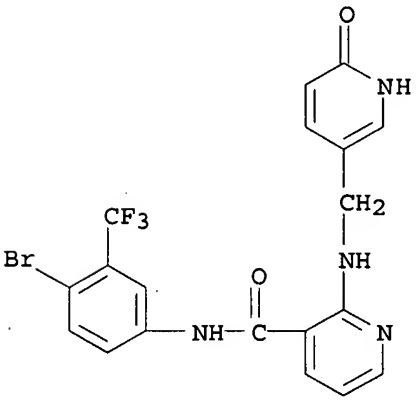


RN 352227-88-4 HCAPLUS
CN 3-Pyridinecarboxamide, 2-[[(6-methoxy-3-pyridinyl)methyl]amino]-N-[4-(1-propynyl)-3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

Updated Search



RN 352227-93-1 HCAPLUS
CN 3-Pyridinecarboxamide, N-[4-bromo-3-(trifluoromethyl)phenyl]-2-[[(1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]- (9CI) (CA INDEX NAME)



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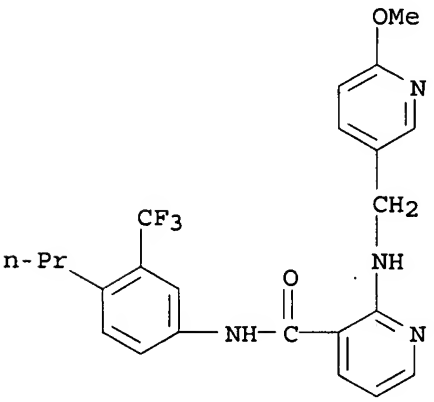
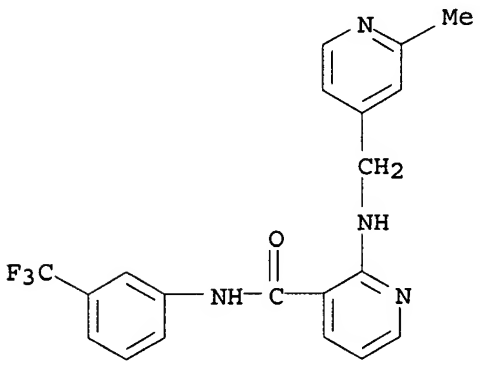


IT 352227-58-8P 352227-90-8P 352227-91-9P

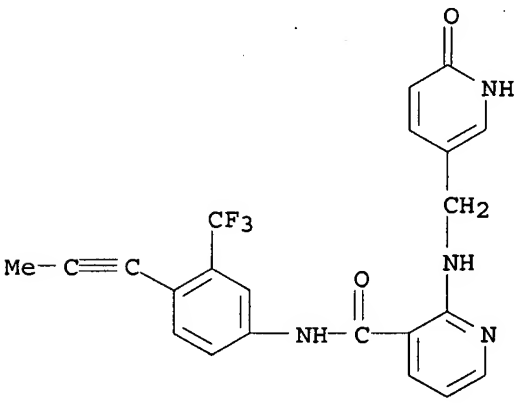
Updated Search

352227-94-2P 352227-95-3P 352227-96-4P
352228-08-1P 352228-09-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-aminonicotinamides as VEGF-receptor tyrosine kinase inhibitors)

RN 352227-58-8 HCAPLUS
CN 3-Pyridinecarboxamide, 2-[[(2-methyl-4-pyridinyl)methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 352227-90-8 HCAPLUS
CN 3-Pyridinecarboxamide, 2-[[(1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[4-(1-propynyl)-3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 352227-91-9 HCAPLUS
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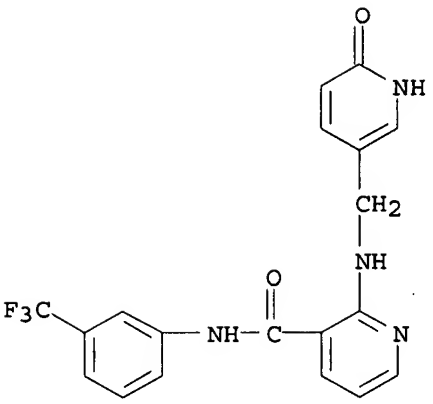
Updated Search



RN 352227-94-2 HCAPLUS
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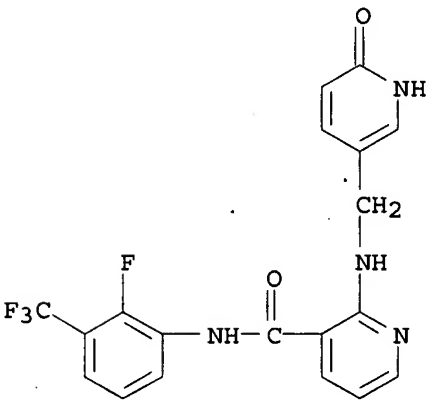

RN 352227-95-3 HCAPLUS
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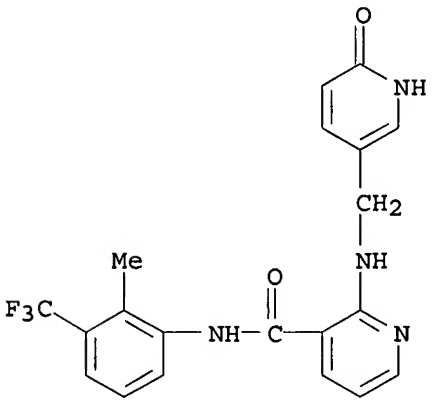
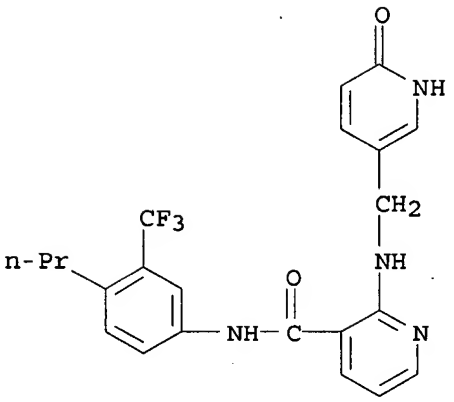


RN 352227-96-4 HCAPLUS
CN 3-Pyridinecarboxamide, 2-[[(1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[4-propyl-3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

Updated Search



RN 352228-08-1 HCAPLUS
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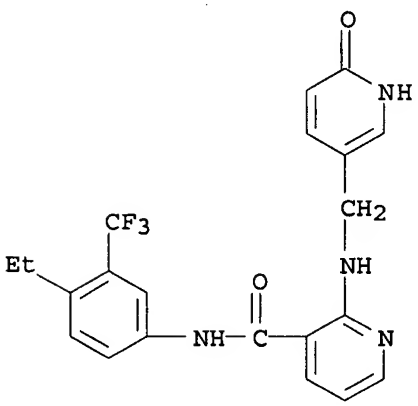
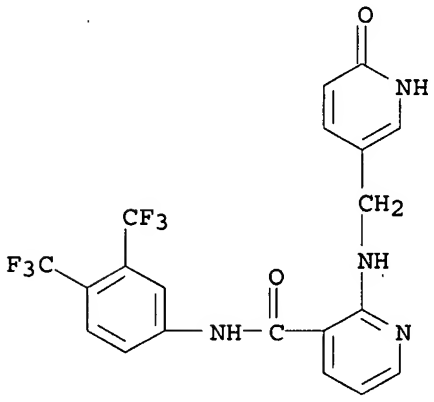


RN 352228-09-2 HCAPLUS
CN 3-Pyridinecarboxamide, N-[3,4-bis(trifluoromethyl)phenyl]-2-[[(1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS

Updated Search

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:335388 HCAPLUS
DOCUMENT NUMBER: 132:347491
TITLE: Preparation of N-aryl(thio)anthranilic acid amides as VEGF receptor tyrosine kinase inhibitors
INVENTOR(S): Altmann, Karl-Heinz; Bold, Guido; Furet, Pascal; Manley, Paul William; Wood, Jeanette Marjorie; Ferrari, Stefano; Hofmann, Francesco; Mestan, Jurgen; Huth, Andreas; Kruger, Martin; Seidelmann, Dieter; Menrad, Andreas; Haberey, Martin; Thierauch, Karl-Heinz
PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis-Erfindungen Verwaltungsgesellschaft m.b.H.; Schering Aktiengesellschaft
SOURCE: PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000027820	A1	20000518	WO 1999-EP8545	19991108
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
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BR 9915210	A	20010724	BR 1999-15210	19991108
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EP 1129075	A1	20010905	EP 1999-971802	19991108
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JP 2002529453	T	20020910	JP 2000-581000	19991108
AU 758230	B2	20030320	AU 2000-13811	19991108
NZ 511339	A	20030725	NZ 1999-511339	19991108
RU 2286338	C2	20061027	RU 2001-114978	19991108
NO 2001001894	A	20010704	NO 2001-1894	20010417
ZA 2001003290	A	20030123	ZA 2001-3290	20010423
MX 2001PA04256	A	20030606	MX 2001-PA4256	20010427
US 2002019414	A1	20020214	US 2001-850434	20010507
US 6448277	B2	20020910		
IN 2001CN00638	A	20050304	IN 2001-CN638	20010508
ZA 2001004673	A	20020909	ZA 2001-4673	20010607
US 2003064992	A1	20030403	US 2002-180289	20020626
US 6878720	B2	20050412		
US 2004198782	A1	20041007	US 2004-828951	20040421
US 7002022	B2	20060221		
US 2006074112	A1	20060406	US 2005-254897	20051020

PRIORITY APPLN. INFO.:		
GB 1998-24579	A	19981110
WO 1999-EP8545	W	19991108
US 2001-850434	A3	20010507
US 2002-180289	A3	20020626

Updated Search

OTHER SOURCE(S): MARPAT 132:347491

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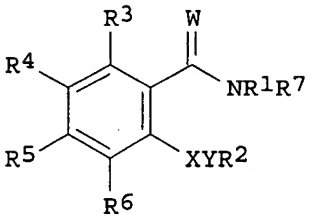


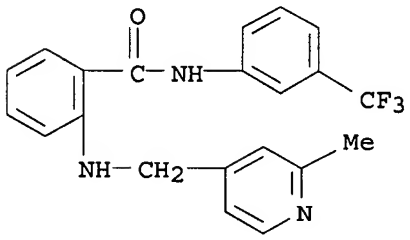
I

AB Use of title compds. I; W = O, S; X = NR8; Y = CR9R10(CH2)n, SO2; R9, R10 = H, alkyl; n = 0-3; R1 = aryl; R2 = mono- or bicyclic heteroaryl with the exception that R2 cannot = 2-phthalimidyl, and when Y = SO2 cannot represent 2,1,3-benzothiadiazol-4-yl; R3-R6 = H, substituent; R7, R8 = H, alkyl; or a N-oxide or a pharmaceutically acceptable salt thereof, for the preparation of a pharmaceutical product for the treatment of a neoplastic disease which responds to an inhibition of the VEGF receptor tyrosine kinase activity is claimed. Thus, a mixture of 4-pyridinecarboxaldehyde and 2-amino-N-(4-trifluoromethylphenyl)benzamide (preparation given) in MeOH containing HOAc was treated with NaBH3CN followed by 16 h stirring to give 2-[(4-pyridyl)methyl]amino-N-[4-(trifluoromethyl)phenyl]benzamide. Tested I inhibited Flt-1 VEGF receptor tyrosine kinase with IC50 = 0.18-0.56 μM.

IT 269391-00-6P 269391-01-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N-aryl(thio)anthranilic acid amides as VEGF receptor tyrosine kinase inhibitors)

RN 269391-00-6 HCAPLUS

CN Benzamide, 2-[[(2-methyl-4-pyridinyl)methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 269391-01-7 HCAPLUS

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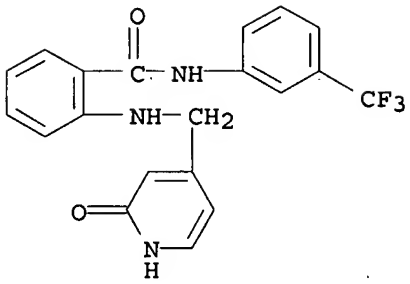
Updated Search



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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FILE 'REGISTRY' ENTERED AT 16:48:04 ON 01 OCT 2007
L1 STRUCTURE UPLOADED
L2 STRUCTURE UPLOADED
L3 8 S L2
L4 207 S L2 FULL

FILE 'HCAPLUS' ENTERED AT 16:54:00 ON 01 OCT 2007
L5 16 S L4
L6 5 S L5 AND BOLD, G?/AU

=> s l5 not l6
L7 11 L5 NOT L6

=> s l7 and furet, p?/au
154 FURET, P?/AU
L8 1 L7 AND FURET, P?/AU

=> d l8, ibib abs hitstr, 1

L8 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1309915 HCAPLUS
DOCUMENT NUMBER: 147:180753
TITLE: Structural biology contributions to the discovery of drugs to treat chronic myelogenous leukemia
AUTHOR(S): Cowan-Jacob, Sandra W.; Fendrich, Gabriele; Floersheimer, Andreas; Furet, Pascal; Liebetanz, Janis; Rummel, Gabriele; Rheinberger, Paul; Centeleghe, Mario; Fabbro, Doriano; Manley, Paul W.
CORPORATE SOURCE: Novartis Institutes for Biomedical Research, Basel, Switz.
SOURCE: Acta Crystallographica, Section D: Biological Crystallography (2007), D63(1), 80-93
CODEN: ABCRE6; ISSN: 0907-4449
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Chronic myelogenous leukemia (CML) results from the Bcr-Abl oncoprotein, which has a constitutively activated Abl tyrosine kinase domain. Although most chronic phase CML patients treated with imatinib as first-line therapy maintain excellent durable responses, patients who have progressed to advanced-stage CML frequently fail to respond or lose their response to

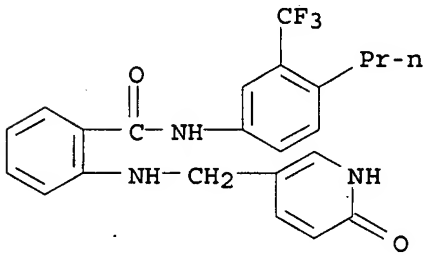
Updated Search

therapy owing to the emergence of drug-resistant mutants of the protein. More than 40 such point mutations have been observed in imatinib-resistant patients. The crystal structures of wild-type and mutant Abl kinase in complex with imatinib and other small-mol. Abl inhibitors were determined, with the aim of understanding the mol. basis of resistance and to aid in the design and optimization of inhibitors active against the resistance mutants. These results are presented in a way which illustrates the approaches used to generate multiple structures, the type of information that can be gained and the way that this information is used to support drug discovery.

IT 709044-90-6, NVP-AEG 082
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(structural biol. contributions to the discovery of drugs to treat chronic myelogenous leukemia)

RN 709044-90-6 HCAPLUS

CN Benzamide, 2-[[(1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[4-propyl-3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L3               8 S L2
L4             207 S L2 FULL

     FILE 'HCAPLUS' ENTERED AT 16:54:00 ON 01 OCT 2007
L5              16 S L4
L6               5 S L5 AND BOLD, G?/AU
L7              11 S L5 NOT L6
L8               1 S L7 AND FURET, P?/AU

=> s l7 not l8
L9              10 L7 NOT L8

=> s l9 and manley, p?/au
            214 MANLEY, P?/AU
L10           0 L9 AND MANLEY, P?/AU

=> d l9, ibib abs hitstr, 1-10

L9   ANSWER 1 OF 10  HCAPLUS  COPYRIGHT 2007 ACS on STN
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Updated Search

ACCESSION NUMBER: 2007:150229 HCAPLUS
DOCUMENT NUMBER: 146:221063
TITLE: Method for assaying anti-tumor effect of angiogenesis inhibitor
INVENTOR(S): Uenaka, Toshimitsu; Yamamoto, Yuji; Matsui, Junji
PATENT ASSIGNEE(S): Eisai R & D Management Co., Ltd., Japan
SOURCE: PCT Int. Appl., 147pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007015578	A1	20070208	WO 2006-JP315698	20060802

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

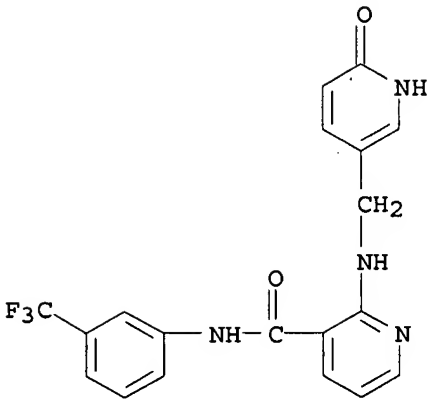
PRIORITY APPLN. INFO.: JP 2005-224173 A 20050802
JP 2006-164700 A 20060614
OTHER SOURCE(S): MARPAT 146:221063

AB Disclosed is a method for predicting the anti-tumor effect of an angiogenesis inhibitor. The method comprises evaluating the EGF-dependence property of an angiogenesis inhibitor with respect to proliferation and/or survival of tumor cells, and using the evaluated EGF-dependence property as a measure. The anti-tumor effect of an angiogenesis inhibitor correlates with the EGF-dependency property of the inhibitor with respect to proliferation and/or survival of tumor cells. Therefore, an angiogenesis inhibitor is capable of exerting an excellent anti-tumor effect by using it in combination with a substance having an EGF inhibitory effect.

IT 352227-91-9, ABP 309
RL: ANT (Analyte); BSU (Biological study, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(method for assaying anti-tumor effect of angiogenesis inhibitor by evaluating EGF-dependency)

RN 352227-91-9 HCAPLUS
CN 3-Pyridinecarboxamide, 2-[[(1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

Updated Search



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:144036 HCAPLUS
DOCUMENT NUMBER: 146:221062
TITLE: Method for predicting antitumor efficacy of angiogenesis inhibitor
INVENTOR(S): Matsui, Junji; Semba, Taro
PATENT ASSIGNEE(S): Eisai R & D Management Co., Ltd., Japan
SOURCE: PCT Int. Appl., 104pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007015569	A1	20070208	WO 2006-JP315563	20060801

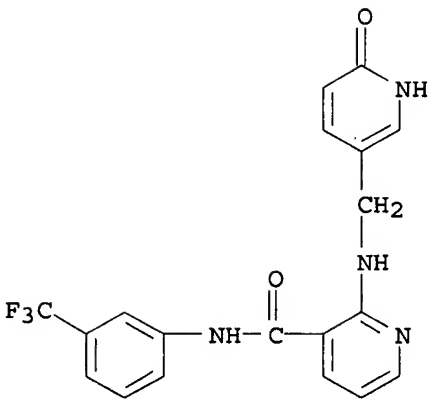
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: JP 2005-223440 A 20050801
OTHER SOURCE(S): MARPAT 146:221062

AB A method for predicting the antitumor efficacy of an angiogenesis inhibitor is provided, which comprises measuring the number of blood vessels surrounded by pericytes in tumor, and using the measurement value as a measure for the anti-tumor effect.

IT 352227-91-9
RL: ANT (Analyte); BSU (Biological study, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(method for predicting antitumor efficacy of angiogenesis inhibitor)
RN 352227-91-9 HCAPLUS
CN 3-Pyridinecarboxamide, 2-[[(1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

Updated Search



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:440299 HCAPLUS
DOCUMENT NUMBER: 144:468030
TITLE: Preparation of novel nicotinamide pyridinureas as vascular endothelial growth factor (VEGF) receptor kinase inhibitors
INVENTOR(S): Bohlmann, Rolf; Haberey, Martin; Hess-Stumpp, Holger; Huth, Andreas; Ince, Stuart; Krueger, Martin; Thierauch, Karl-Heinz
PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006048249	A1	20060511	WO 2005-EP11709	20051028
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
EP 1655297	A1	20060510	EP 2004-90420	20041103
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR, IS, YU				
AU 2005300734	A1	20060511	AU 2005-300734	20051028
CA 2586265	A1	20060511	CA 2005-2586265	20051028
EP 1807416	A1	20070718	EP 2005-806225	20051028
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,				

Updated Search

IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR

US 2006160861	A1	20060720	US 2005-262953		20051101
IN 2007DN02886	A	20070817	IN 2007-DN2886		20070418
PRIORITY APPLN. INFO.:			EP 2004-90420	A	20041103
			US 2004-626918P	P	20041112
			WO 2005-EP11709	W	20051028

OTHER SOURCE(S): CASREACT 144:468030; MARPAT 144:468030

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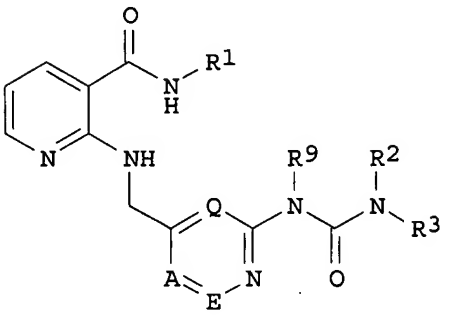

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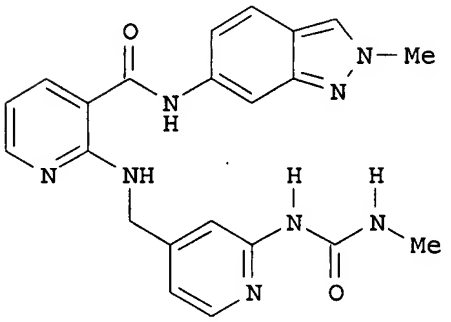


II

AB The title compds. I [A, E and Q = CH or N (only maximum of 2 N atoms are contained in the ring); R1 = (un)substituted (hetero)aryl; R2, R3, R9 = H, alkyl, haloalkyl, etc.; or R9 = H, and NR2R3 = (un)substituted 3-8 membered heterocycloalkyl, preferably 4-7 membered heterocycloalkyl, more preferably 5-6 membered heterocycloalkyl; or R3 = H, alkyl, alkoxyalkyl, and R2 and R9 together with the two N atoms to which they are attached form 5-7 membered ring, preferably 5-6 membered ring] which are VEGF receptor kinase inhibitors useful as pharmaceutical agents for preventing or treating diseases that are triggered by persistent angiogenesis, were prepared E.g., a multi-step synthesis of II, starting from 2-chloroisonicotinonitrile, was given. II showed IC50 of 10 nM against KDR kinase (VEGFR-2). Pharmaceutical composition comprising the compound I is disclosed.

IT 886586-76-1P

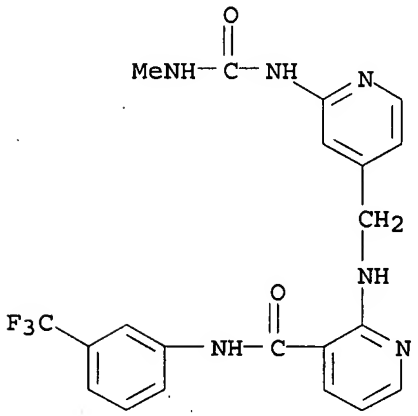
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of novel nicotinamide pyridinureas as VEGF receptor kinase inhibitors for treating and preventing diseases that are triggered by persistent angiogenesis)

RN 886586-76-1 HCAPLUS

Updated Search

CN 3-Pyridinecarboxamide, 2-[[[2-[[(methylamino)carbonyl]amino]-4-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 4 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:268466 HCAPLUS
DOCUMENT NUMBER: 144:324798
TITLE: Simultaneous use of sulfonamide-containing compound and angiogenesis inhibitor
INVENTOR(S): Owa, Takashi; Ozawa, Yoichi; Semba, Taro
PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan
SOURCE: PCT Int. Appl., 270 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006030941	A1	20060323	WO 2005-JP17228	20050913
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
WO 2006030947	A1	20060323	WO 2005-JP17238	20050913
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				

Updated Search

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

US 2006135486	A1	20060622	US 2005-226655	20050913
EP 1797877	A1	20070620	EP 2005-785820	20050913

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU

PRIORITY APPLN. INFO.:	US 2004-609452P	P	20040913
	JP 2005-54150	A	20050228
	JP 2005-54475	A	20050228
	WO 2005-JP17238	W	20050913

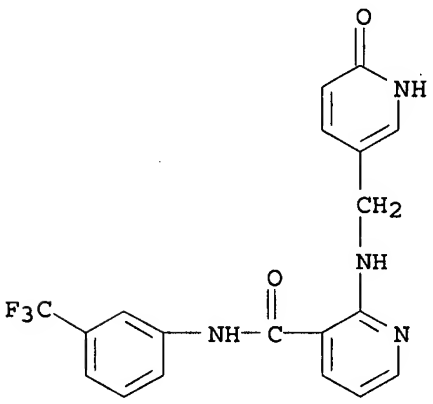
OTHER SOURCE(S): MARPAT 144:324798

AB A pharmaceutical composition comprising a sulfonamide-containing compound combined with an angiogenesis inhibitor.

IT 352227-91-9, ABP 309
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sulfonamide-containing compds. and angiogenesis inhibitors for combination chemotherapy of cancer)

RN 352227-91-9 HCAPLUS

CN 3-Pyridinecarboxamide, 2-[[(1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 5 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	2005:953989 HCAPLUS
DOCUMENT NUMBER:	143:242054
TITLE:	Pharmaceutical combination comprising a CDK inhibitor and a VEGF receptor inhibitor
INVENTOR(S):	Siemeister, Gerhard
PATENT ASSIGNEE(S):	Schering Aktiengesellschaft, Germany
SOURCE:	Eur. Pat. Appl., 40 pp. CODEN: EPXXDW
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

Updated Search

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1568368	A1	20050831	EP 2004-90071	20040226

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

PRIORITY APPLN. INFO.: EP 2004-90071 20040226

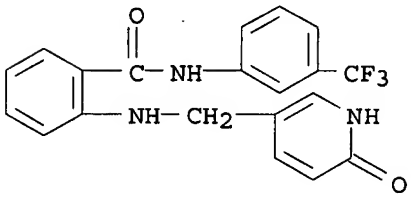
OTHER SOURCE(S): MARPAT 143:242054

AB Pharmaceutical combinations comprising a cyclin-dependent kinase (CDK) inhibitor and a vascular endothelial growth factor receptor (VEGF-R) inhibitor and their use for the treatment of different diseases are described. A CDK inhibitor and a VEGF-R inhibitor are used as a combined preparation simultaneously, sep. or sequentially. For example, a combination of a CDK inhibitor, i.e., N-[5-[[[5-(1,1-dimethylethyl)-2-oxazolyl]methyl]thio]-2-thiazolyl]-4-piperidinecarboxamide and a VEGF-R inhibitor, i.e., (4-chlorophenyl)[4-(4-pyridylmethyl)phthalazin-1-yl]ammonium hydrogen succinate was evaluated in a human estrogen-independent mammary carcinoma model, xenografted in mice. The combination of both compds. at a dosing of 10 mg/kg i.p. once daily for the CDK inhibitor and 50 mg/kg per orally twice daily for the VEGF-R inhibitor showed a clear, synergistic or substantially greater, inhibition of tumor growth in comparison to monotherapy and the control group. The results show that a combination therapy using a CDK inhibitor and VEGF-R inhibitor was substantially superior in the efficacy of tumor growth inhibition as compared to monotherapy with the each of the sep. compds.

IT 524941-35-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination comprising CDK inhibitor and VEGF receptor inhibitor for treatment or prophylaxis of various diseases)

RN 524941-35-3 HCAPLUS

CN Benzamide, 2-[[(1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 6 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:1127340 HCAPLUS

DOCUMENT NUMBER: 142:74461

TITLE: Preparation of pyridonylmethyl anthranylamides as inhibitors of vascular endothelial growth factor receptors VEGFR-2 and VEGFR-3.

INVENTOR(S): Huth, Andreas; Krueger, Martin; Zorn, Ludwig; Ince, Stuart; Bohlmann, Rolf; Thierauch, Karl-Heinz; Menrad, Andreas; Haberey, Martin; Hess-Stumpp, Holger

PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany

SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

Updated Search

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004111005	A1	20041223	WO 2004-EP6236	20040609
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
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DE 10327719	A1	20050120	DE 2003-10327719	20030613
AU 2004247377	A1	20041223	AU 2004-247377	20040609
CA 2526041	A1	20041223	CA 2004-2526041	20040609
EP 1633713	A1	20060315	EP 2004-739742	20040609
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
CN 1805936	A	20060719	CN 2004-80016364	20040609
BR 2004011360	A	20060725	BR 2004-11360	20040609
JP 2006527228	T	20061130	JP 2006-515873	20040609
US 2005049281	A1	20050303	US 2004-866078	20040614
US 7202260	B2	20070410		
IN 2005DN05428	A	20070817	IN 2005-DN5428	20051124
MX 2005PA13586	A	20060309	MX 2005-PA13586	20051213
NO 2006000196	A	20060112	NO 2006-196	20060112
US 2007135489	A1	20070614	US 2007-654643	20070118
PRIORITY APPLN. INFO.:			DE 2003-10327719 A	20030613
			US 2003-482009P P	20030625
			WO 2004-EP6236 W	20040609
			US 2004-866078 A3	20040614

OTHER SOURCE(S): MARPAT 142:74461

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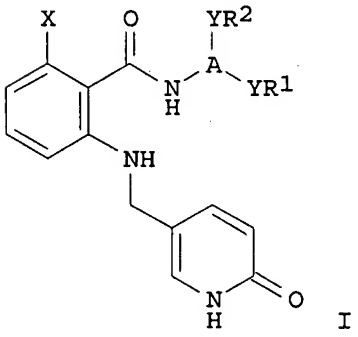


I

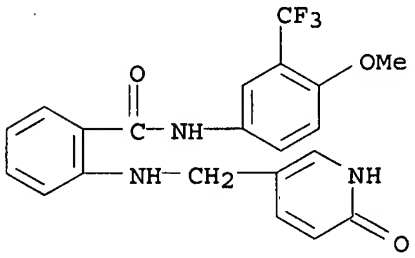
AB Title compds. (I; A = aryl, heteroaryl; X = H, F; R1, R2 = H, halo, alkyl, alkoxyalkyl, haloalkyl, cycloalkyl, halocycloalkyl; Y = bond, O, S, SO, SO2), were prepared Thus, 2-[(6-oxo-1,6-dihydropyridin-3-ylmethyl)amino]benzoic acid (preparation given), N-methylmorpholine, 4-trifluoromethoxyaniline, and HATU were stirred 2.5 h in CH2Cl2 at room temp and 1.5 h at 100° bath temperature to give 50.1% 2-[(6-oxo-1,6-dihydropyridin-3-ylmethyl)amino]-N-(4-

Updated Search

trifluoromethoxyphenyl)benzamide. The latter inhibited VEGFR II with IC50 = 180 nM. The invention relates to selected anthranylamide pyridones that inhibit VEGFR-2 and VEGFR-3 and to their use as medicaments for treating diseases that are triggered by persistent angiogenesis.

IT 811805-34-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyridonylmethyl anthranylamides as inhibitors of vascular endothelial growth factor receptors VEGFR-2 and VEGFR-3)

RN 811805-34-2 HCAPLUS
CN Benzamide, 2-[[(1,6-dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[4-methoxy-3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 7 OF 10 HCAPLUS COPYRIGHT 2007 ACS.on STN
ACCESSION NUMBER: 2004:120827 HCAPLUS
DOCUMENT NUMBER: 140:181330
TITLE: Preparation of anthranylamidopyridines as inhibitors of vascular endothelial growth factor receptor-2 and -3 (VEGFR-2 and -3).
INVENTOR(S): Huth, Andreas; Krueger, Martin; Zorn, Ludwig; Ince, Stuart; Thierauch, Karl-Heinz; Menrad, Andreas; Haberey, Martin; Hess-Stump, Holger
PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 88 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004013102	A1	20040212	WO 2003-EP7964	20030722
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10235690	A1	20040219	DE 2002-10235690	20020731
DE 10328036	A1	20050105	DE 2003-10328036	20030619

Updated Search

CA 2493026	A1	20040212	CA 2003-2493026		20030722
AU 2003281855	A1	20040223	AU 2003-281855		20030722
BR 2003013122	A	20050705	BR 2003-13122		20030722
CN 1671666	A	20050921	CN 2003-818334		20030722
EP 1594841	A1	20051116	EP 2003-740470		20030722
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JP 2005538112	T	20051215	JP 2004-525272		20030722
NZ 537291	A	20070223	NZ 2003-537291		20030722
US 2004147535	A1	20040729	US 2003-631018		20030731
US 7148357	B2	20061212			
US 2005054654	A1	20050310	US 2004-870491		20040618
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NO 2005001035	A	20050429	NO 2005-1035		20050225
US 2007015794	A1	20070118	US 2006-525091		20060922
PRIORITY APPLN. INFO.:			DE 2002-10235690	A	20020731
			DE 2003-10328036	A	20030619
			US 2002-407970P	P	20020905
			US 2003-483896P	P	20030702
			WO 2003-EP7964	W	20030722
			US 2003-631018	A3	20030731

OTHER SOURCE(S): MARPAT 140:181330

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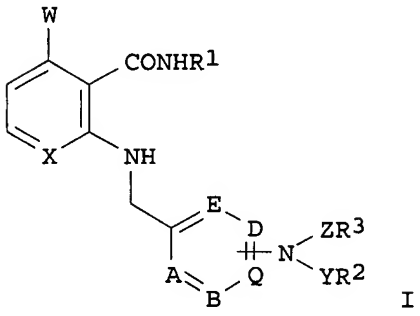


I

AB Title compds. [I; X = CH, N; W = H, F; A, B, D, E, Q = N, C; ≤2 of A, B, D, E, Q = N; R1 = (substituted) aryl, heteroaryl; Y, Z = bond, CO, CS, SO2; R2, R3 = H, CONR9R10, SO2R6, COR11, NR9R10, (substituted) alkyl, cycloalkyl, cycloalkenyl, aryl, heteroaryl; R2YNZAR3 = atoms to form a 3-8 membered (substituted) (unsatd.) ring; R6 = H, alkyl, haloalkyl, (substituted) aryl, heteroaryl, NR9R10; R9, R10 = H, alkyl, alkenyl, aryl, cycloalkyl, etc.; R11 = alkyl, alkoxy, hydroxyalkyl, hydroxyalkoxy, cycloalkyl, (substituted) Ph, pyridyl, biphenyl, naphthyl], were prepared Thus, 2-[(2-bromopyridin-4-ylmethyl)amino]-N-(3-trifluoromethylphenyl)benzamide (preparation given) pyridine, and N,N-dimethylaminoethylamine were heated in a pressure vessel for 5 h at 200° to give 2-[[2-(2-dimethylaminoethylamino)pyridin-4-ylmethyl]amino]-N-(3-trifluoromethylphenyl)benzamide. I inhibited VEGFR-2 with IC50 = 8-65 nM. I can be used for treatment of tumor or metastasis growth, psoriasis, Kaposi's sarcoma, restenosis, endometriosis, Crohn's disease, Hodgkin's disease, leukemia, arthritis, hemangioma, angiofibroma, eye disease, renal diseases, transplant rejection, fibrotic diseases, mesangial cell proliferative diseases, atherosclerosis, injuries to nervous tissue and for inhibition of the reocclusion of vessels after balloon catheter treatment, in vessel prosthetics, or after the application of mech. devices to hold open vessels, as immunosuppressants,

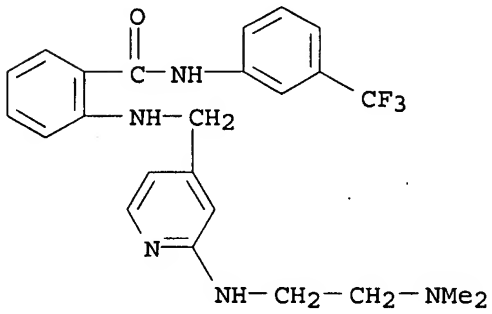
Updated Search

for scar-free wound healing, age spots and contact dermatitis.

IT 657399-79-6P, 2-[[2-(2-Dimethylaminoethylamino)pyridin-4-ylmethyl]amino]-N-(3-trifluoromethylphenyl)benzamide 657399-81-0P 657399-82-1P 657399-83-2P 657399-84-3P 657399-85-4P 657399-87-6P 657399-88-7P 657399-93-4P 657399-97-8P 657399-98-9P 657399-99-0P 657400-00-5P 657400-01-6P 657400-02-7P 657400-03-8P 657400-04-9P 657400-05-0P 657400-06-1P 657400-07-2P 657400-08-3P 657400-09-4P 657400-10-7P 657400-11-8P 657400-12-9P 657400-37-8P 657400-38-9P 657400-39-0P 657400-40-3P 657400-41-4P 657400-43-6P 657400-44-7P 657400-45-8P 657400-47-0P 657400-48-1P 657400-51-6P 657400-53-8P 657400-63-0P 657400-64-1P 657400-74-3P 657400-75-4P 657400-95-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of anthranylamidopyridines as inhibitors of vascular endothelial growth factor receptor)

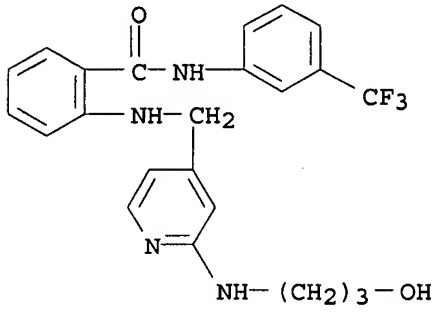
RN 657399-79-6 HCAPLUS

CN Benzamide, 2-[[[2-[[2-(dimethylamino)ethyl]amino]-4-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 657399-81-0 HCAPLUS

CN Benzamide, 2-[[[2-[(3-hydroxypropyl)amino]-4-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 657399-82-1 HCAPLUS

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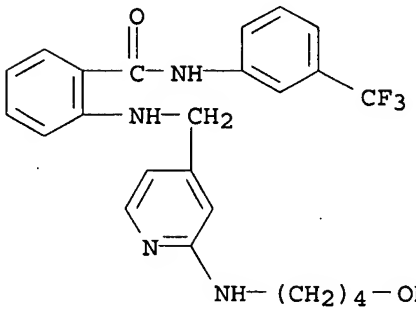
Updated Search

(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 657399-83-2 HCAPLUS
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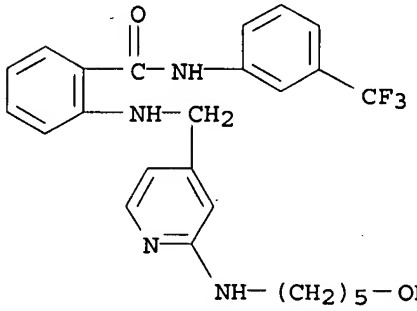

RN 657399-84-3 HCAPLUS
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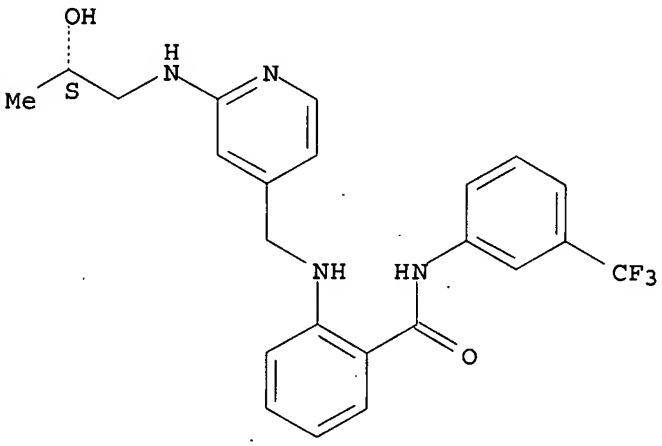
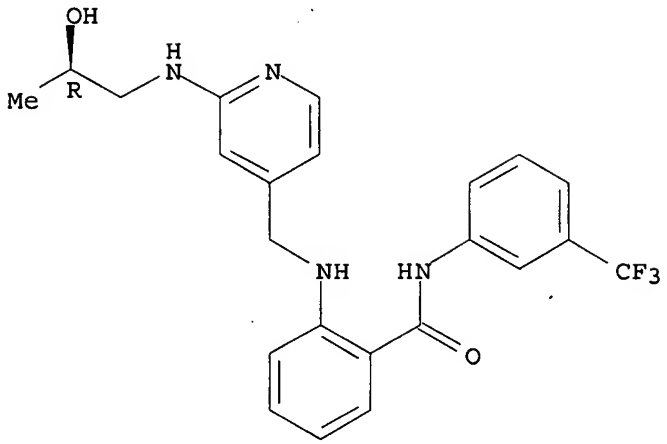
Absolute stereochemistry.



RN 657399-85-4 HCAPLUS
CN Benzamide, 2-[[[2-[[(2R)-2-hydroxypropyl]amino]-4-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

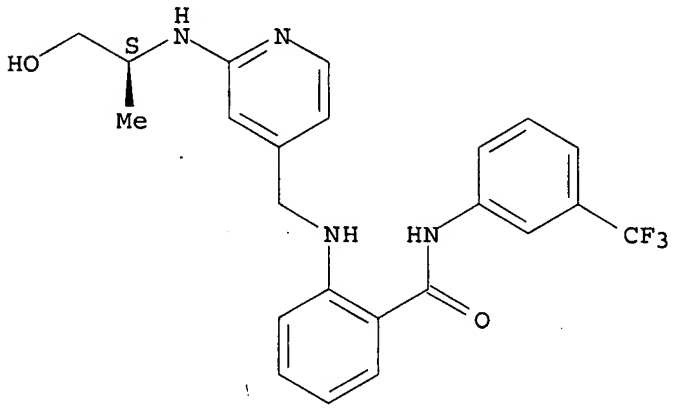
Updated Search

Absolute stereochemistry.



RN 657399-87-6 HCAPLUS
CN Benzamide, 2-[[[2-[[(1S)-2-hydroxy-1-methylethyl]amino]-4-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 657399-88-7 HCAPLUS
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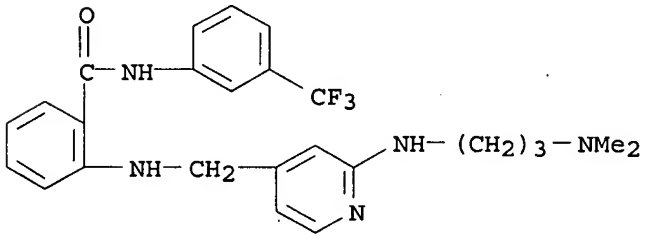
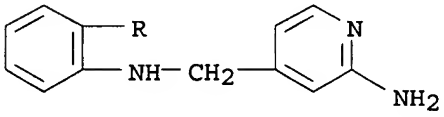
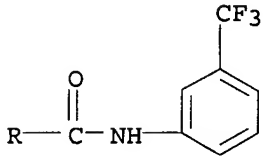


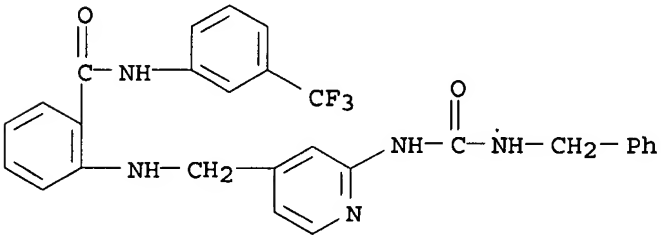
Updated Search

RN 657399-93-4 HCAPLUS
CN Benzamide, 2-[[(2-amino-4-pyridinyl)methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)





RN 657399-97-8 HCAPLUS
CN Benzamide, 2-[[[2-[[[(phenylmethyl)amino]carbonyl]amino]-4-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 657399-98-9 HCAPLUS
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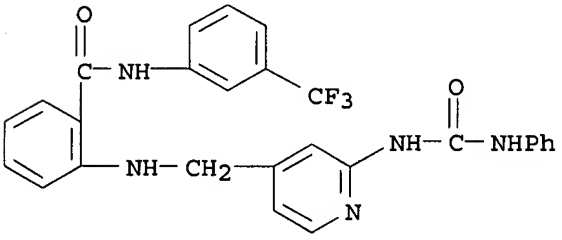

RN 657399-99-0 HCAPLUS
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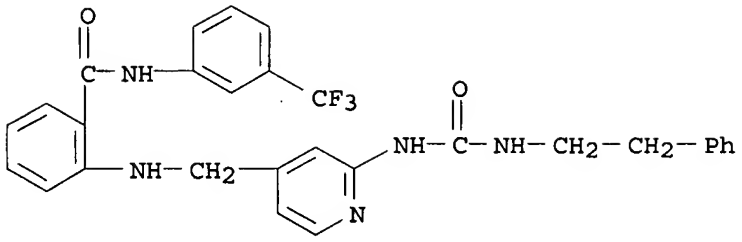
Updated Search



RN 657400-00-5 HCAPLUS
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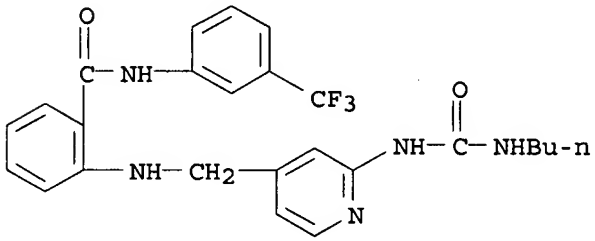

RN 657400-01-6 HCAPLUS
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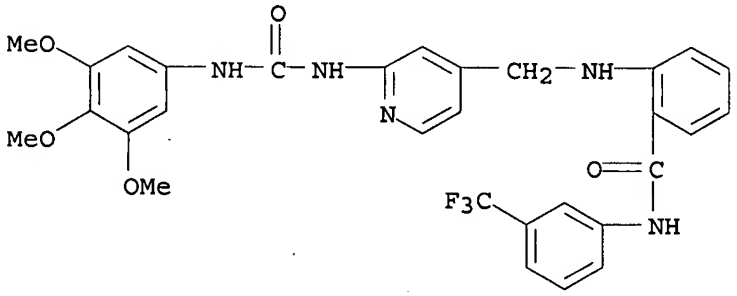
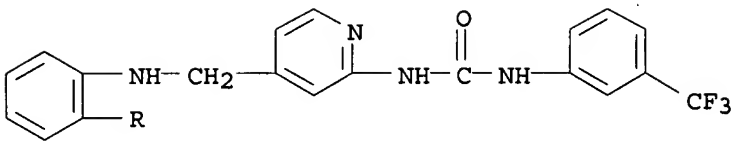
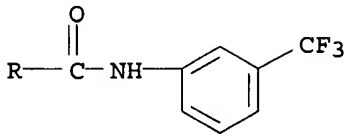


RN 657400-02-7 HCAPLUS
CN Benzamide, N-[3-(trifluoromethyl)phenyl]-2-[[[2-[[[[3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-4-pyridinyl]methyl]amino]- (9CI) (CA INDEX NAME)

Updated Search





RN 657400-03-8 HCAPLUS
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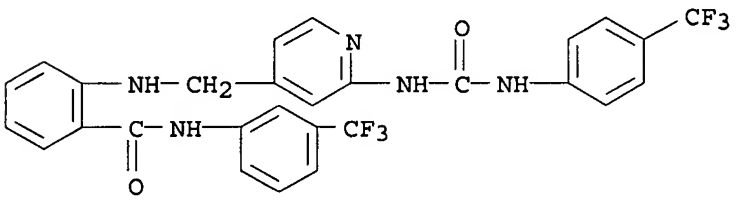

RN 657400-04-9 HCAPLUS
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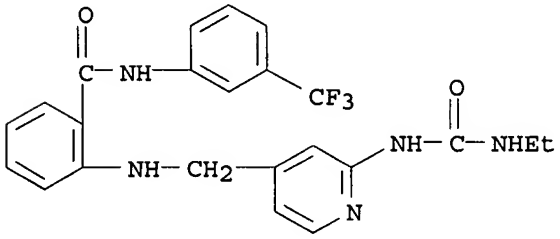
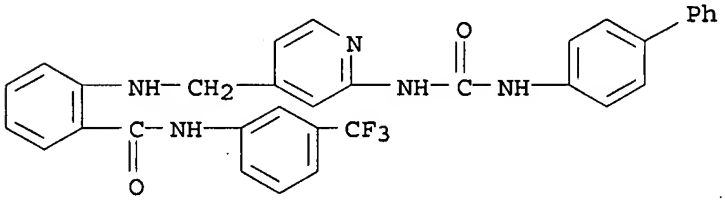
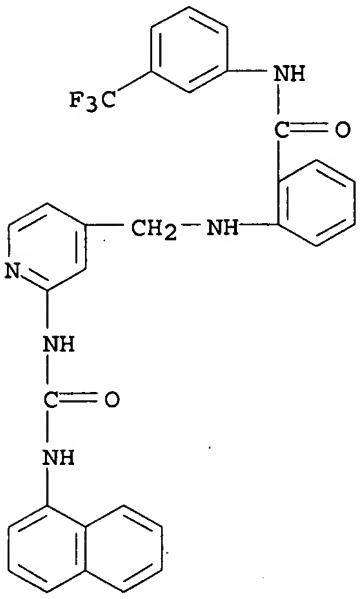


RN 657400-05-0 HCAPLUS
CN Benzamide, 2-[[[2-[[([1,1'-biphenyl]-4-ylamino)carbonyl]amino]-4-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

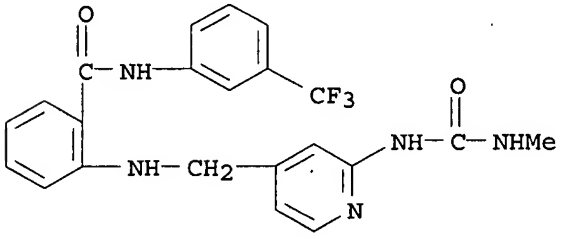


Updated Search

RN 657400-06-1 HCAPLUS
CN Benzamide, 2-[[[2-[[(1-naphthalenylamino)carbonyl]amino]-4-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 657400-07-2 HCAPLUS
CN Benzamide, 2-[[[2-[[(methylamino)carbonyl]amino]-4-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 657400-08-3 HCAPLUS
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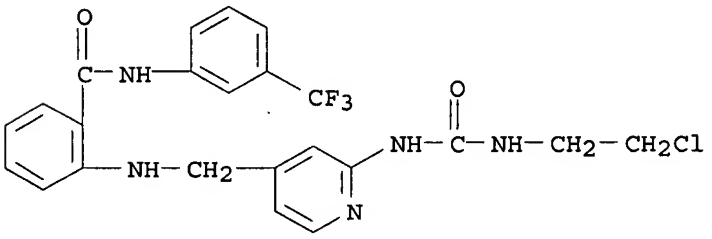

Updated Search

RN 657400-09-4 HCAPLUS
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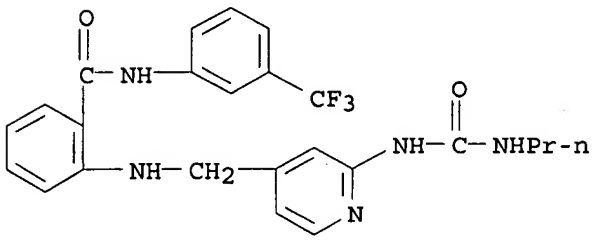

RN 657400-10-7 HCAPLUS
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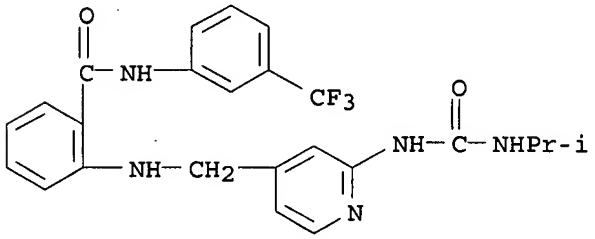

RN 657400-11-8 HCAPLUS
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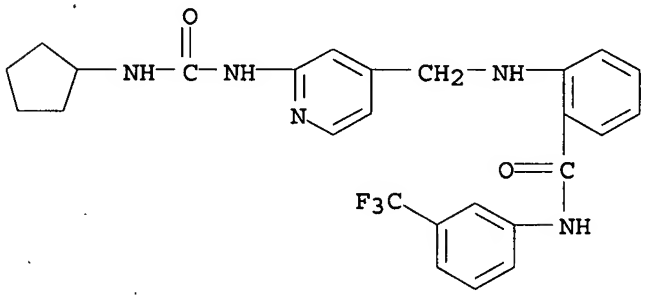

RN 657400-12-9 HCAPLUS
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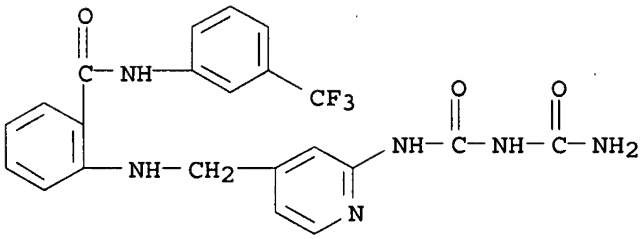
Updated Search



RN 657400-37-8 HCAPLUS
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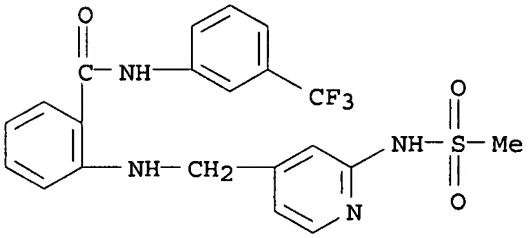

RN 657400-38-9 HCAPLUS
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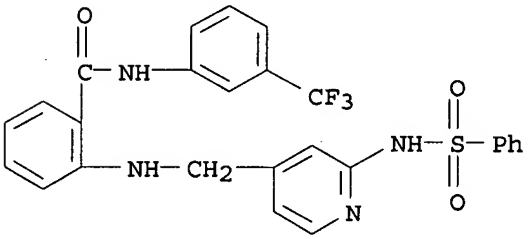

RN 657400-39-0 HCAPLUS
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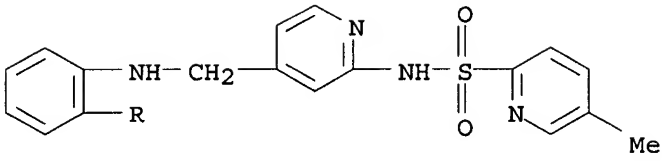
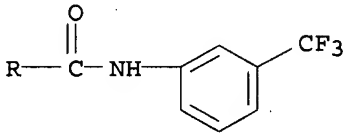
Updated Search





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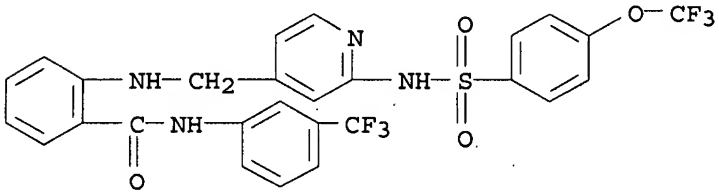
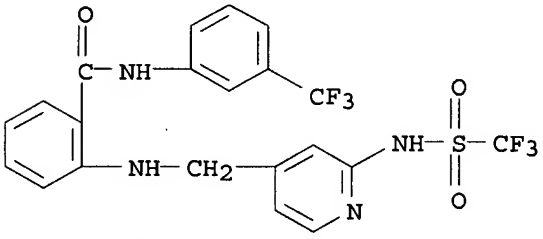
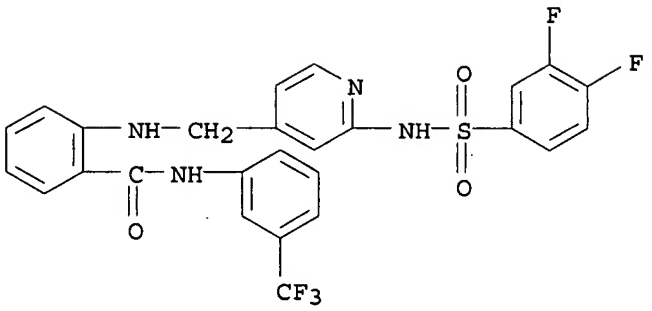


RN 657400-41-4 HCAPLUS
CN Benzamide, N-[3-(trifluoromethyl)phenyl]-2-[[[2-[[(trifluoromethyl)sulfonyl]amino]-4-pyridinyl]methyl]amino]- (9CI) (CA INDEX NAME)



RN 657400-43-6 HCAPLUS
CN Benzamide, 2-[[[2-[[(3,4-difluorophenyl)sulfonyl]amino]-4-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

Updated Search



RN 657400-44-7 HCAPLUS
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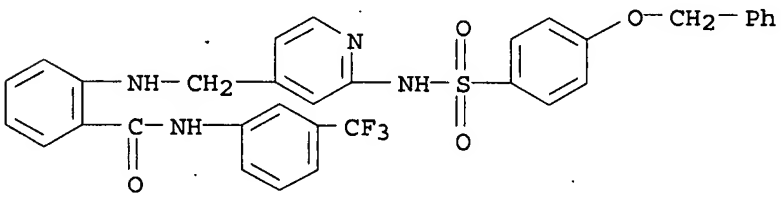

RN 657400-45-8 HCAPLUS
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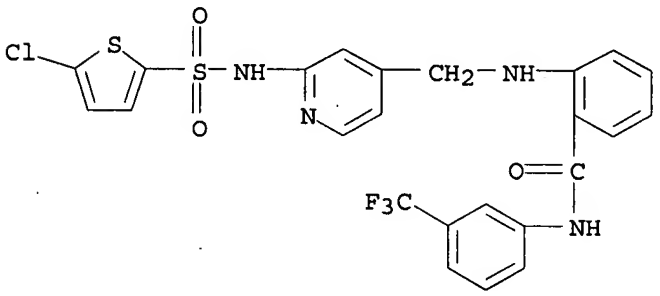

RN 657400-47-0 HCAPLUS
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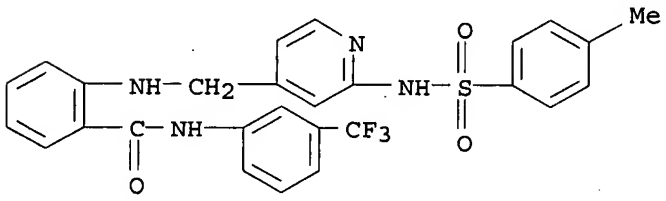

Updated Search

RN 657400-48-1 HCAPLUS
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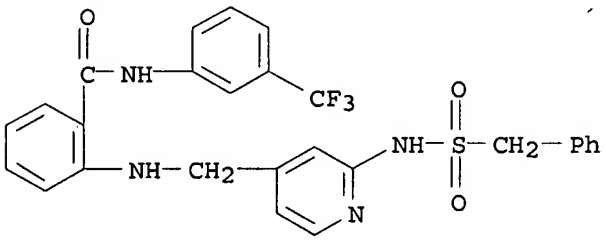

RN 657400-51-6 HCAPLUS
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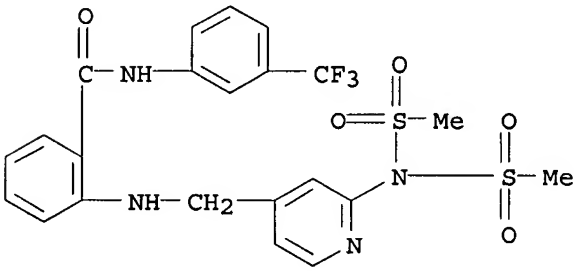
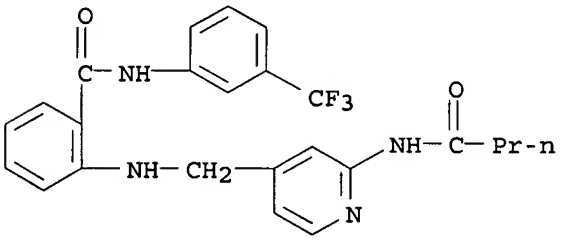
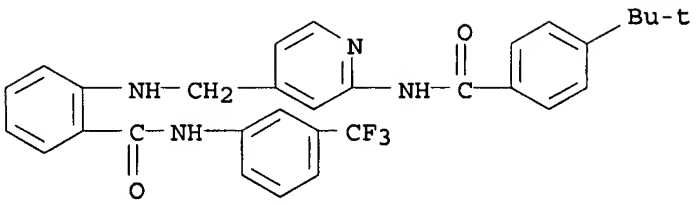


RN 657400-53-8 HCAPLUS
CN Benzamide, 2-[[[2-[(1-oxobutyl)amino]-4-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 657400-63-0 HCAPLUS
CN Benzamide, 2-[[[2-[[4-(1,1-dimethylethyl)benzoyl]amino]-4-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

Updated Search



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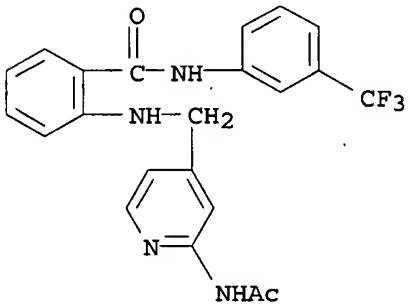
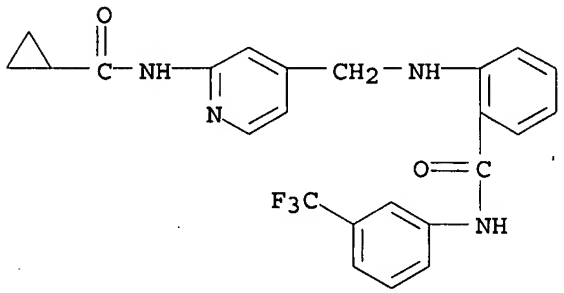


RN 657400-74-3 HCAPLUS
CN Benzamide, 2-[[[2-[(cyclopropylcarbonyl)amino]-4-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 657400-75-4 HCAPLUS
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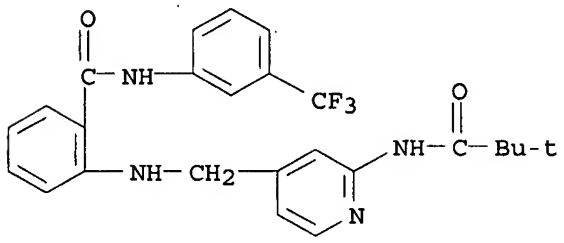

Updated Search

RN 657400-95-8 HCAPLUS
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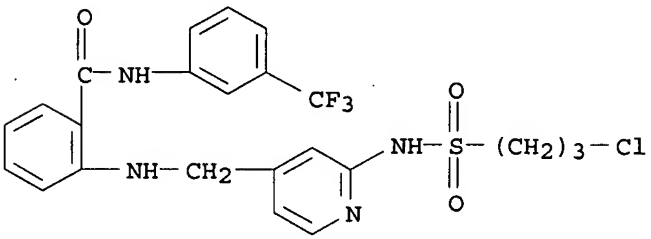
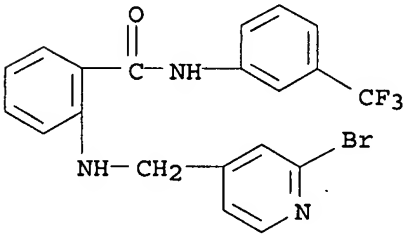


IT 657401-06-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of anthranylamidopyridines as inhibitors of vascular endothelial growth factor receptor)
RN 657401-06-4 HCAPLUS
CN Benzamide, 2-[[(2-bromo-4-pyridinyl)methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



L9 ANSWER 8 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:950057 HCAPLUS
DOCUMENT NUMBER: 140:16647
TITLE: Preparation of 2-aminopyridine-3-carboxamides as remedies for angiogenesis mediated diseases
INVENTOR(S): Askew, Benny; Adams, Jeffrey; Booker, Shon; Chen, Guoqing; DiPietro, Lucian V.; Elbaum, Daniel; Germain, Julie; Geuns-Meyer, Stephanie D.; Habgood, Gregory J.; Handley, Michael; Huang, Qi; Kim, Tae-seong; Li, Aiwen; Nishimura, Nobuko; Nomak, Rana; Patel, Vinod F.; Riahi, Babak; Kim, Joseph L.; Xi, Ning; Yang, Kevin; Yuan, Chester Chenguang
PATENT ASSIGNEE(S): Amgen Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 252 pp., Cont.-in-part of U.S. Ser. No. 46,681.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

Updated Search

US 2003225106	A1	20031204	US 2002-197974		20020717
US 6878714	B2	20050412			
US 2003125339	A1	20030703	US 2002-46681		20020110
US 6995162	B2	20060207			
AT 361288	T	20070515	AT 2002-717325		20020111
EP 1798230	A1	20070620	EP 2007-3413		20020111
R: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE, TR, AL, LT, LV, MK, RO, SI					
ZA 2003005197	A	20040319	ZA 2003-5197		20030704
CA 2492100	A1	20040122	CA 2003-2492100		20030715
WO 2004007458	A1	20040122	WO 2003-US22417		20030715
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BG 108012	A	20041130	BG 2003-108012		20030721
US 2005261313	A1	20051124	US 2004-14184		20041215
MX 2005PA00584	A	20050419	MX 2005-PA584		20050113
US 2006040956	A1	20060223	US 2005-234713		20050923
AU 2006200437	A1	20060223	AU 2006-200437		20060201
PRIORITY APPLN. INFO.:			US 2001-261339P	P	20010112
			US 2001-323764P	P	20010919
			US 2002-46681	A2	20020110
			AU 2002-248340	A3	20020111
			EP 2002-717325	A3	20020111
			US 2002-197974	A	20020717
			WO 2003-US22417	W	20030715

OTHER SOURCE(S): MARPAT 140:16647

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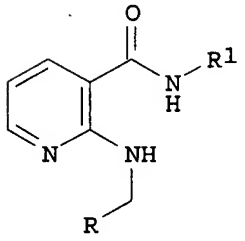

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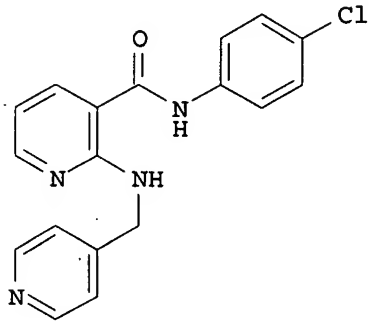


II

AB The title compds. [I; R = (un)substituted 4-pyridyl, 2-pyridyl, 4-pyrimidinyl, 4-quinolyl, etc.; R1 = (un)substituted aryl, cycloalkyl, 5-6 membered heteroaryl, 9-10 membered bicyclic and 11-14 membered tricyclic heterocyclyl], which are effective for prophylaxis and treatment

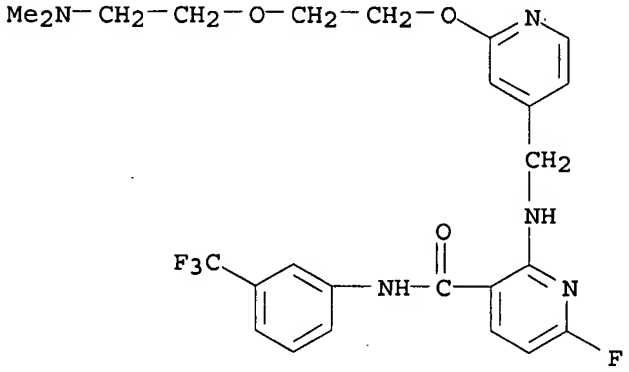
Updated Search

of diseases and other maladies or conditions involving, cancer and the like, were prepared Thus, the title compound II was prepared from 2-aminonicotinic acid, 4-chloroaniline, and 4-pyridinecarboxaldehyde. The compds. I showed inhibition of KDR kinase at < 50 μM. Many compds. I inhibited VEGF-stimulated HUVEC proliferation at a level below 50 nM. Pharmaceutical composition comprising the compound I is claimed.

IT 453563-07-0P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 2-aminopyridine-3-carboxamides for treating angiogenesis mediated diseases)

RN 453563-07-0 HCAPLUS

CN 3-Pyridinecarboxamide, 2-[[[2-[2-[2-(dimethylamino)ethoxy]ethoxy]-4-pyridinyl]methyl]amino]-6-fluoro-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



IT 453561-97-2P 453563-29-6P 453563-38-7P
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453563-75-2P 453563-83-2P 453563-98-9P
453564-12-0P 453564-27-7P 453564-30-2P
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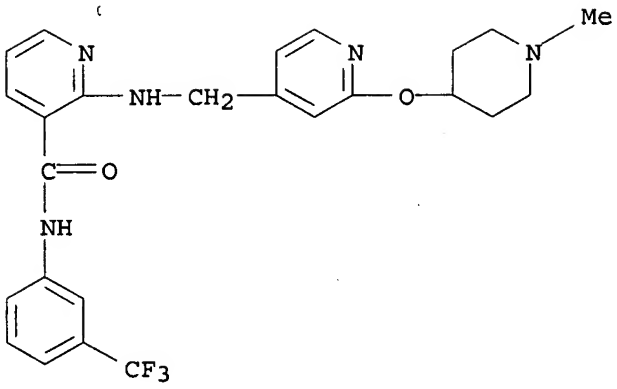
629650-89-1P 629650-90-4P 629650-93-7P
629650-94-8P 629651-03-2P 629651-05-4P
629651-53-2P 629651-58-7P 629651-99-6P
629652-02-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-aminopyridine-3-carboxamides for treating angiogenesis mediated diseases)

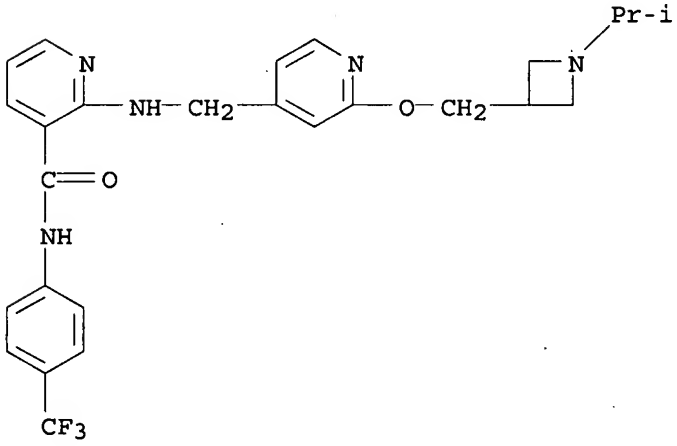
RN 453561-97-2 HCAPLUS

CN 3-Pyridinecarboxamide, 2-[[[2-[(1-methyl-4-piperidinyl)oxy]-4-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

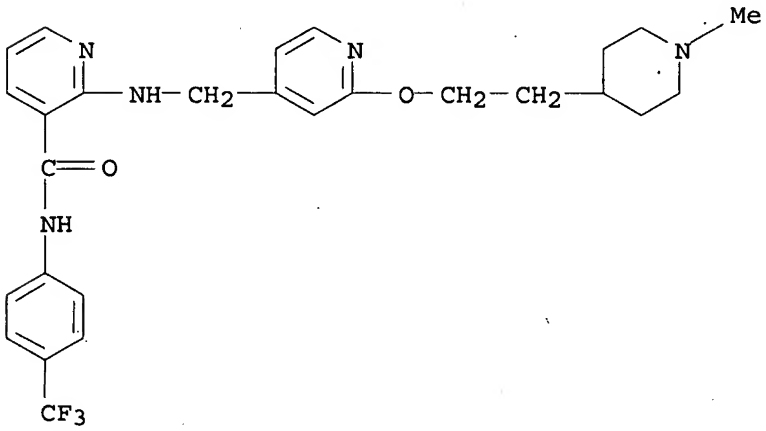
Updated Search



RN 453563-29-6 HCAPLUS
CN 3-Pyridinecarboxamide, 2-[[[2-[[1-(1-methylethyl)-3-azetidinyl]methoxy]-4-pyridinyl]methyl]amino]-N-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 453563-38-7 HCAPLUS
CN 3-Pyridinecarboxamide, 2-[[[2-[2-(1-methyl-4-piperidinyl)ethoxy]-4-pyridinyl]methyl]amino]-N-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



Updated Search

RN 453563-56-9 HCAPLUS
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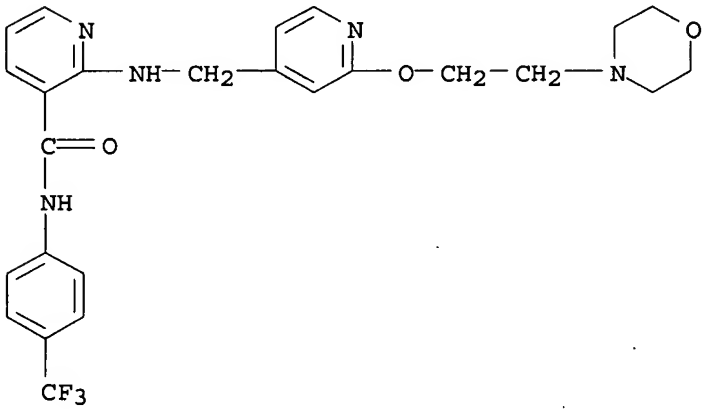

RN 453563-57-0 HCAPLUS
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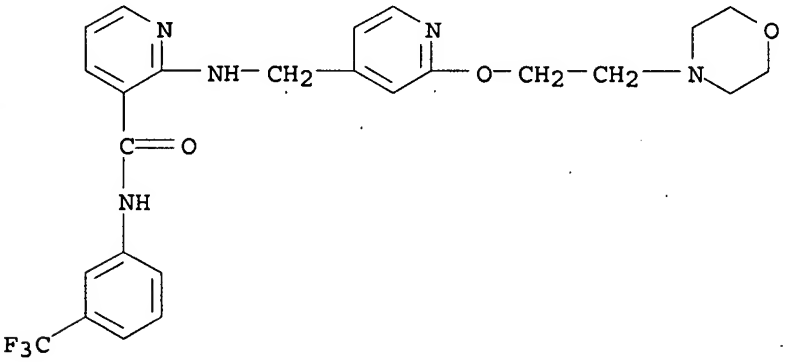
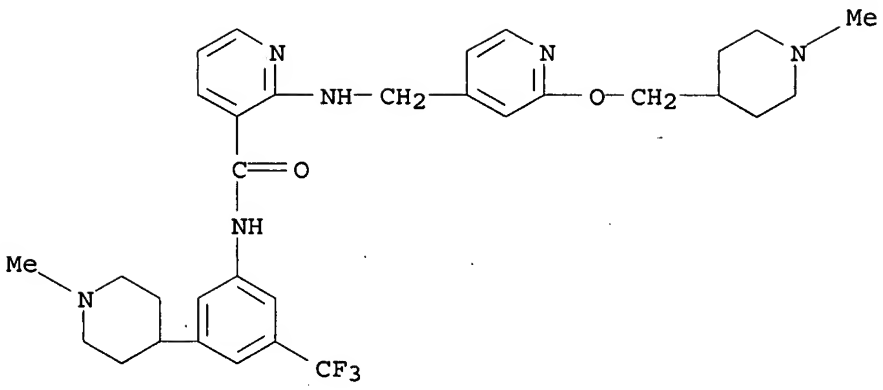
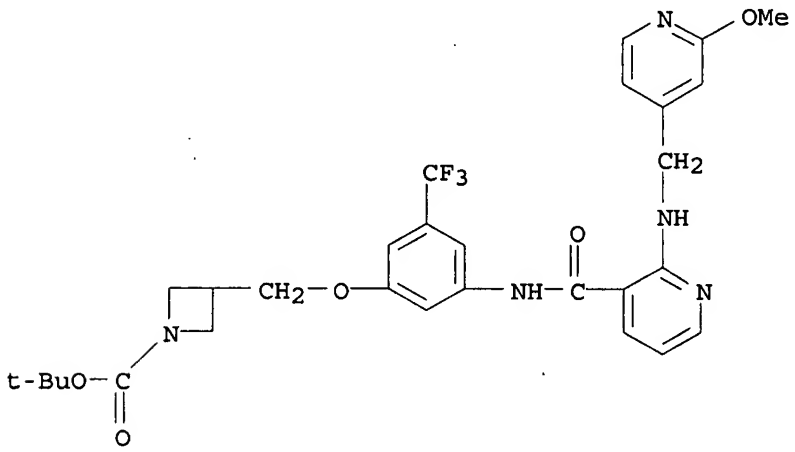


RN 453563-72-9 HCAPLUS
CN 3-Pyridinecarboxamide, 2-[[[2-[(1-methyl-4-piperidinyl)methoxy]-4-pyridinyl]methyl]amino]-N-[3-(1-methyl-4-piperidinyl)-5-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

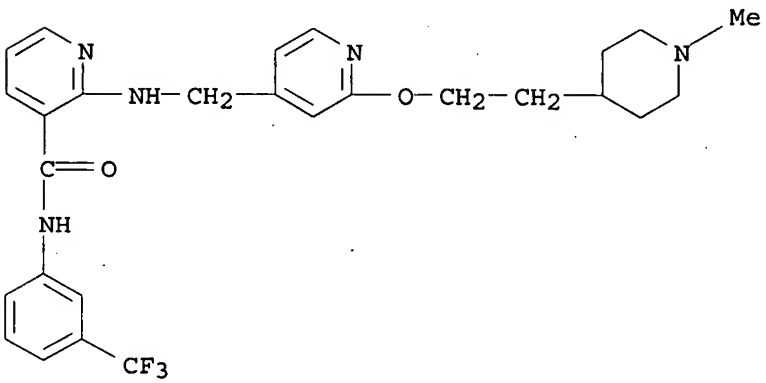
Updated Search



RN 453563-75-2 HCAPLUS
CN 1-Azetidinecarboxylic acid, 3-[[3-[[[2-[[(2-methoxy-4-pyridinyl)methyl]amino]-3-pyridinyl]carbonyl]amino]-5-(trifluoromethyl)phenoxy]methyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

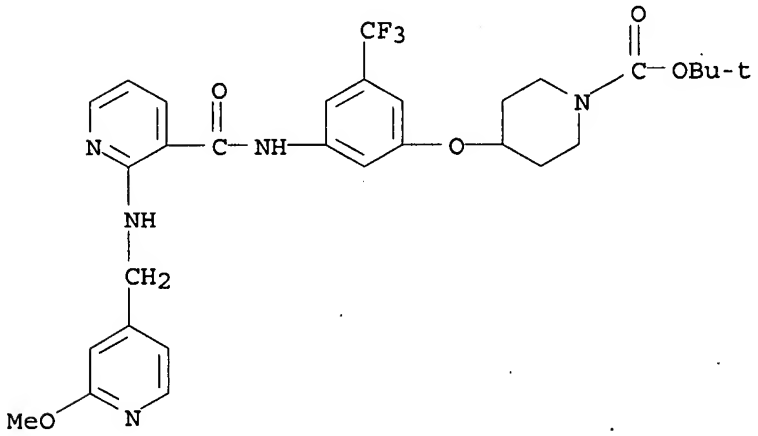


RN 453563-83-2 HCAPLUS
CN 3-Pyridinecarboxamide, 2-[[[2-[2-(1-methyl-4-piperidinyl)ethoxy]-4-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



Updated Search

RN 453563-98-9 HCAPLUS
CN 1-Piperidinecarboxylic acid, 4-[3-[[[2-[[(2-methoxy-4-pyridinyl)methyl]amino]-3-pyridinyl]carbonyl]amino]-5-(trifluoromethyl)phenoxy]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 453564-12-0 HCAPLUS
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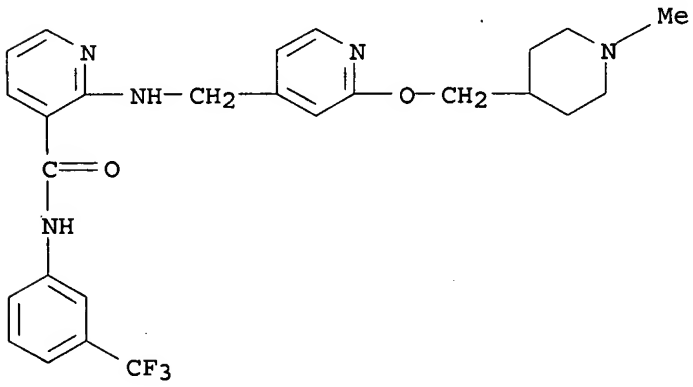
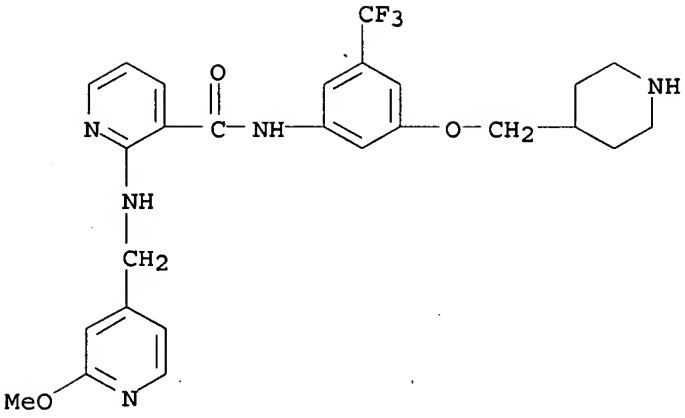


RN 453564-27-7 HCAPLUS
CN 3-Pyridinecarboxamide, 2-[[(2-methoxy-4-pyridinyl)methyl]amino]-N-[3-(4-piperidinylmethoxy)-5-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

Updated Search



RN 453564-30-2 HCAPLUS
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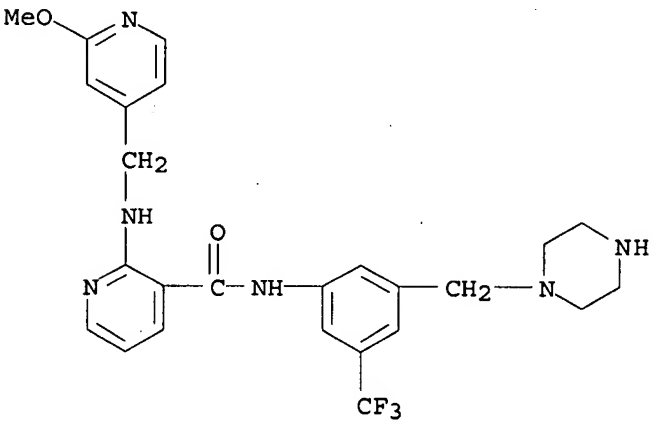
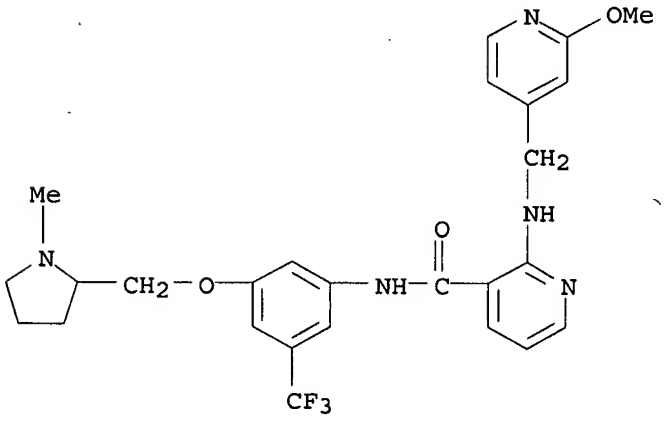


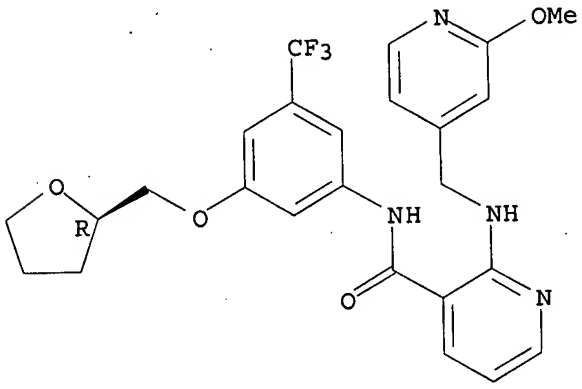
RN 453564-80-2 HCAPLUS
CN 3-Pyridinecarboxamide, 2-[[(2-methoxy-4-pyridinyl)methyl]amino]-N-[3-[(1-methyl-2-pyrrolidinyl)methoxy]-5-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



Updated Search

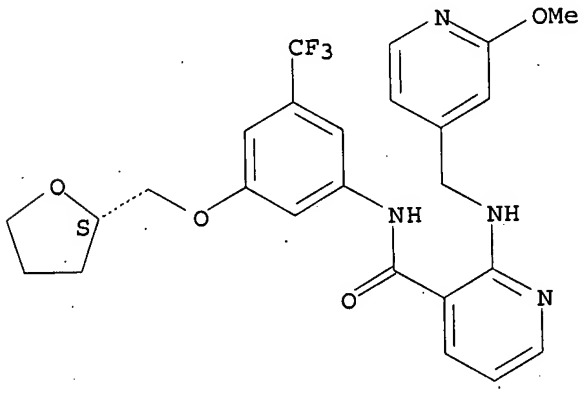
RN 629650-87-9 HCAPLUS
CN 3-Pyridinecarboxamide, 2-[[(2-methoxy-4-pyridinyl)methyl]amino]-N-[3-[[(2R)-tetrahydro-2-furanyl]methoxy]-5-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 629650-88-0 HCAPLUS
CN 3-Pyridinecarboxamide, 2-[[(2-methoxy-4-pyridinyl)methyl]amino]-N-[3-[[(2S)-tetrahydro-2-furanyl]methoxy]-5-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

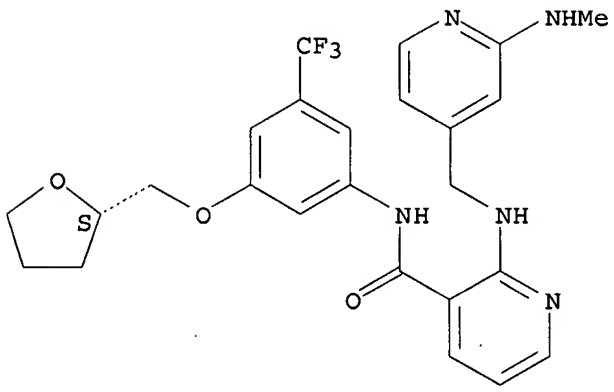
Absolute stereochemistry.



RN 629650-89-1 HCAPLUS
CN 3-Pyridinecarboxamide, 2-[[[2-(methylamino)-4-pyridinyl]methyl]amino]-N-[3-[[(2S)-tetrahydro-2-furanyl]methoxy]-5-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

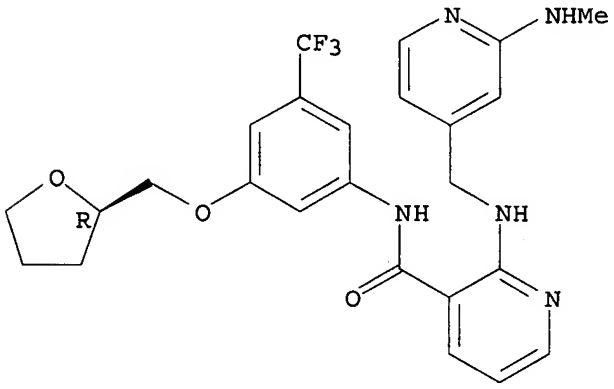
Absolute stereochemistry.

Updated Search



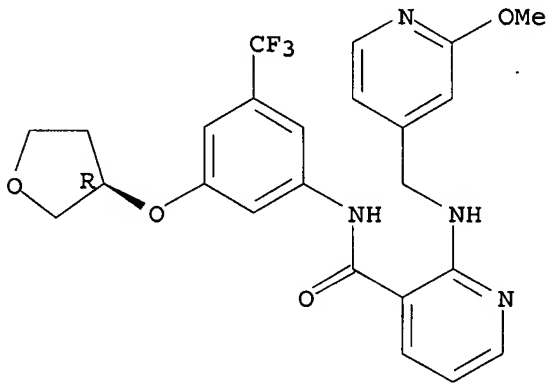
RN 629650-90-4 HCAPLUS
CN 3-Pyridinecarboxamide, 2-[[[2-(methylamino)-4-pyridinyl]methyl]amino]-N-[3-[[(2R)-tetrahydro-2-furanyl]methoxy]-5-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 629650-93-7 HCAPLUS
CN 3-Pyridinecarboxamide, 2-[[(2-methoxy-4-pyridinyl)methyl]amino]-N-[3-[[(3R)-tetrahydro-3-furanyl]oxy]-5-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

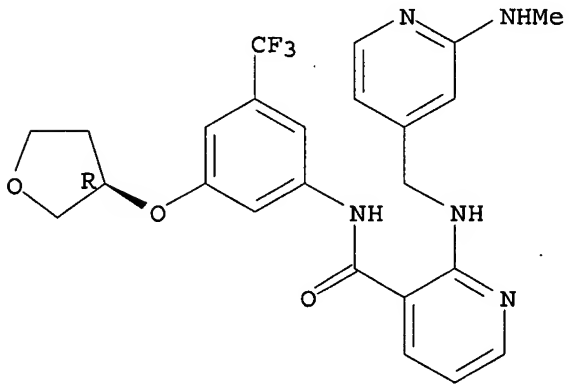
Absolute stereochemistry.



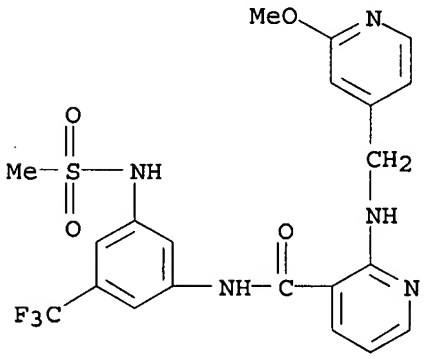
Updated Search

RN 629650-94-8 HCAPLUS
CN 3-Pyridinecarboxamide, 2-[[[2-(methylamino)-4-pyridinyl]methyl]amino]-N-[3-[[(3R)-tetrahydro-3-furanyl]oxy]-5-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

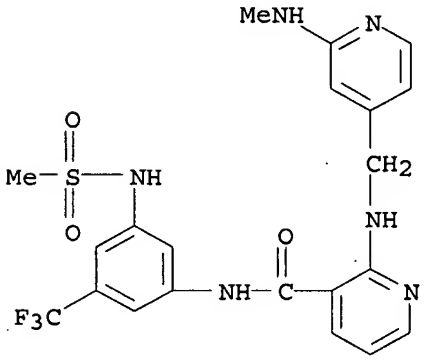
Absolute stereochemistry.



RN 629651-03-2 HCAPLUS
CN 3-Pyridinecarboxamide, 2-[[(2-methoxy-4-pyridinyl)methyl]amino]-N-[3-[(methylsulfonyl)amino]-5-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



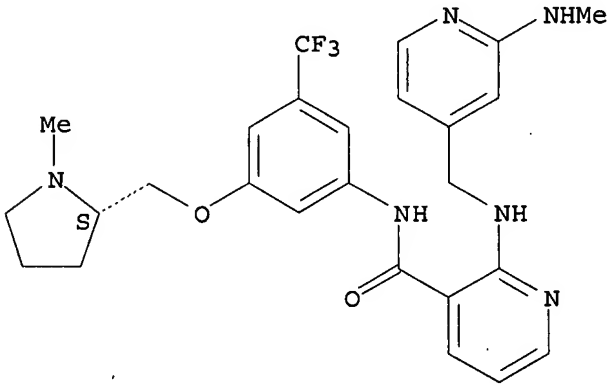
RN 629651-05-4 HCAPLUS
CN 3-Pyridinecarboxamide, 2-[[[2-(methylamino)-4-pyridinyl]methyl]amino]-N-[3-[(methylsulfonyl)amino]-5-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



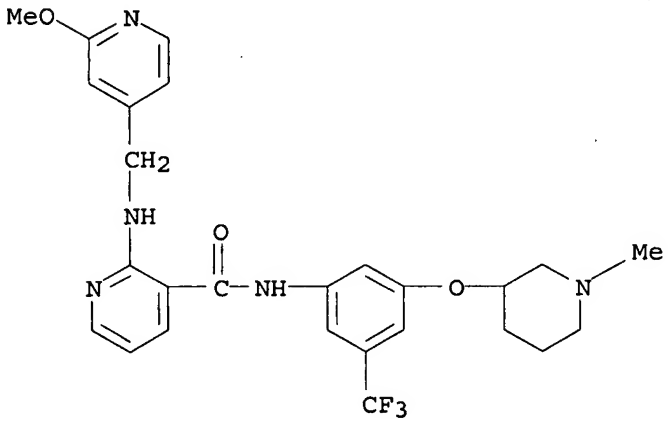
Updated Search

RN 629651-53-2 HCAPLUS
CN 3-Pyridinecarboxamide, 2-[[[2-(methylamino)-4-pyridinyl]methyl]amino]-N-[3-[[(2S)-1-methyl-2-pyrrolidinyl]methoxy]-5-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

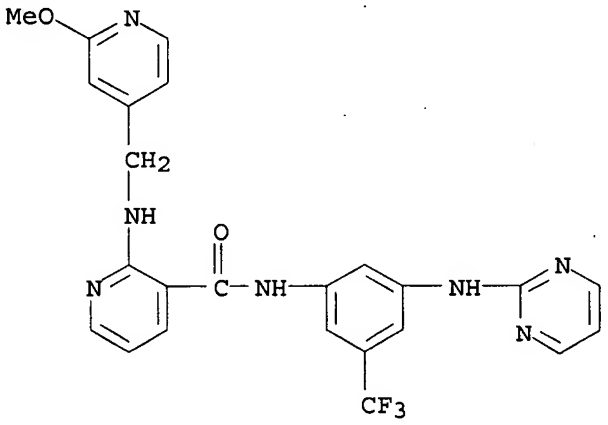


RN 629651-58-7 HCAPLUS
CN 3-Pyridinecarboxamide, 2-[[(2-methoxy-4-pyridinyl)methyl]amino]-N-[3-[(1-methyl-3-piperidinyl)oxy]-5-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



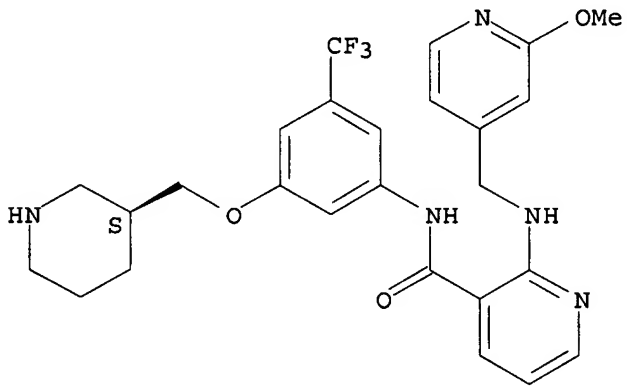
RN 629651-99-6 HCAPLUS
CN 3-Pyridinecarboxamide, 2-[[(2-methoxy-4-pyridinyl)methyl]amino]-N-[3-(2-pyrimidinylamino)-5-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

Updated Search



RN 629652-02-4 HCAPLUS
CN 3-Pyridinecarboxamide, 2-[[(2-methoxy-4-pyridinyl)methyl]amino]-N-[3-[(3S)-3-piperidinylmethoxy]-5-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 9 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:868928 HCAPLUS
DOCUMENT NUMBER: 137:352900
TITLE: Selective anthranilamide pyridine amides as inhibitors of VEGFR-2 and VEGFR-3
INVENTOR(S): Ernst, Alexander; Huth, Andreas; Krueger, Martin; Thierauch, Karl-Heinz; Menrad, Andreas; Haberey, Martin
PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 115 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002090352	A2	20021114	WO 2002-EP4924	20020503

Updated Search

WO 2002090352 A3 20030501
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			DE 2001-10164590	A	20011221
			WO 2002-EP4924	W	20020503

OTHER SOURCE(S): MARPAT 137:352900

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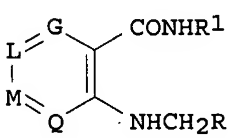

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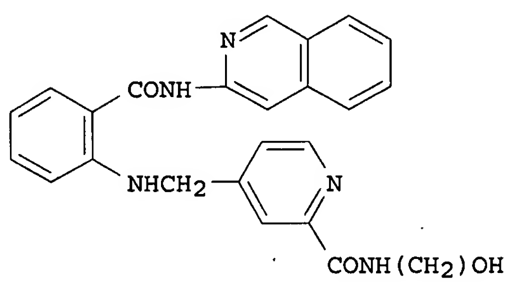


II

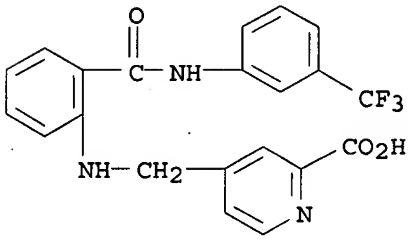
AB Title compds. I [G, L, M, Q = N, (un)substituted CH, ≤1 of them being N; R = (un)substituted N heterocycle; R1 = (un)substituted alkyl, alkenyl, cycloalkyl, cycloalkenyl, aryl, heteroaryl] were prepared I are inhibitors of VEGFR-2 and VEGFR-3 and are used as medicaments for treating diseases that are caused by persistent angiogenesis, such as psoriasis, Kaposi's sarcoma, restenosis, such as e.g. stent-induced restenosis, endometriosis, Crohn's disease, Hodgkin's disease, leukemia, arthritis, such as rheumatoid arthritis, hemangioma, angiofibromatosis, in eye diseases such as diabetic retinopathy, neovascular glaucoma, in kidney diseases such as glomerulonephritis, diabetic nephropathy, malign. nephrosclerosis, thrombic micro-angiopathic syndrome, transplant rejection and glomerulopathy, in fibrotic diseases such as hepatic cirrhosis, mesangial-cell proliferative diseases, arteriosclerosis, damage to the

nerve tissue and inhibition of the re-occlusion of vessels after balloon catheter treatment, in vessel prosthetics or after the use of mech. devices for keeping vessels open, e.g. stents, as immunosuppressants, to support wound healing without scars and in cases of age spots and contact dermatitis. I can also be used as inhibitors of VEGFR-3 in lymphangiogenesis for hyperplastic and dysplastic changes in the lymphatic system. Thus, 2-amino-N-isoquinolin-3-ylbenzamide was treated with 2-bromo-5-pyridinecarboxaldehyde, followed by carboxylaton and amidation to give the amide II. II had IC50 for inhibition of VEGFR-2 of 40 nM and for inhibition of cytochrome 450 isoenzyme 2C9 of 2.9 μM.

IT 474799-40-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of isoquinolinylcarbamoylphenylaminomethylpyridinecarboxamides as VEGFR-2 and VEGFR-3 inhibitors)

RN 474799-40-1 HCAPLUS

CN 2-Pyridinecarboxylic acid, 4-[[[2-[[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]- (9CI) (CA INDEX NAME)



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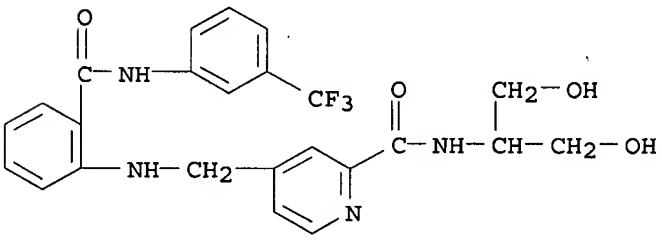
474798-83-9P 474798-84-0P 474798-85-1P
474798-86-2P 474798-87-3P 474798-88-4P
474798-89-5P 474798-90-8P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of isoquinolinylcarbamoylphenylaminomethylpyridinecarboxamides as VEGFR-2 and VEGFR-3 inhibitors)

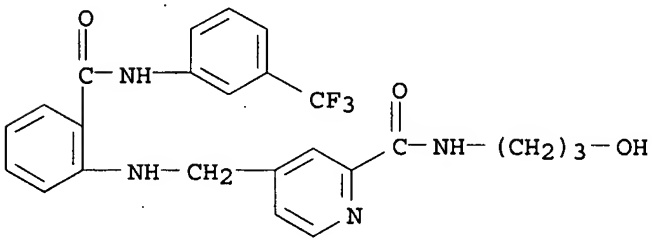
RN 474798-53-3 HCAPLUS

CN 2-Pyridinecarboxamide, N-[2-hydroxy-1-(hydroxymethyl)ethyl]-4-[[[2-[[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]- (9CI) (CA INDEX NAME)

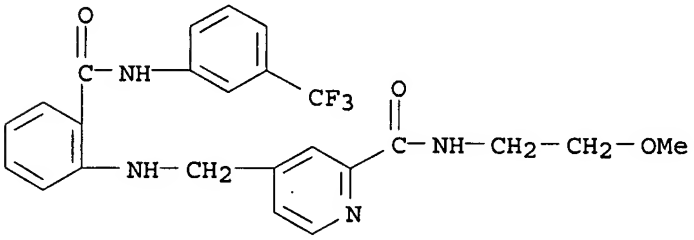


Updated Search

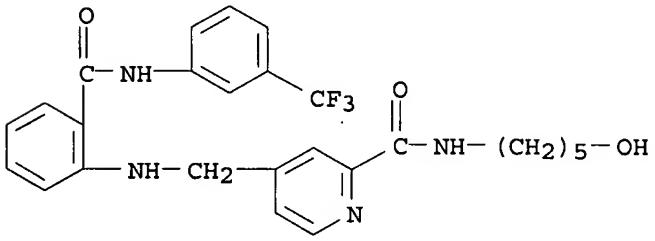
RN 474798-54-4 HCAPLUS
CN 2-Pyridinecarboxamide, N-(3-hydroxypropyl)-4-[[[2-[[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]- (9CI) (CA INDEX NAME)



RN 474798-55-5 HCAPLUS
CN 2-Pyridinecarboxamide, N-(2-methoxyethyl)-4-[[[2-[[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]- (9CI) (CA INDEX NAME)

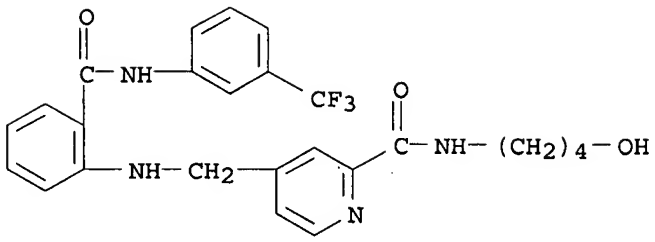


RN 474798-56-6 HCAPLUS
CN 2-Pyridinecarboxamide, N-(5-hydroxypentyl)-4-[[[2-[[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]- (9CI) (CA INDEX NAME)



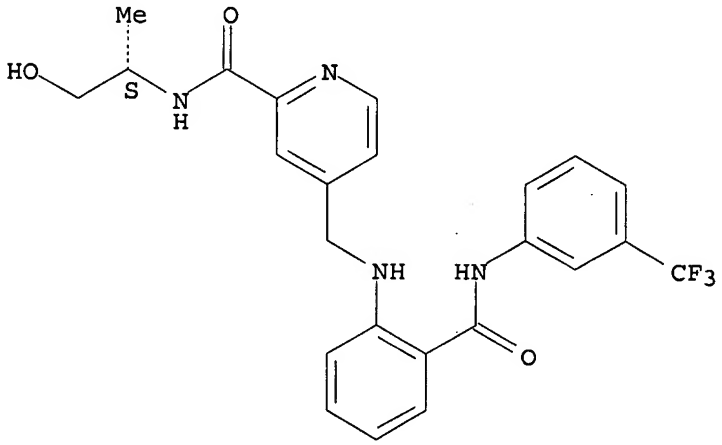
RN 474798-57-7 HCAPLUS
CN 2-Pyridinecarboxamide, N-(4-hydroxybutyl)-4-[[[2-[[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]- (9CI) (CA INDEX NAME)

Updated Search



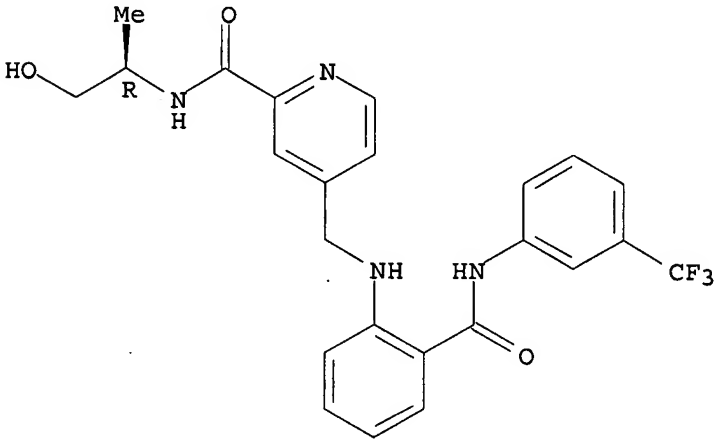
RN 474798-58-8 HCAPLUS
CN 2-Pyridinecarboxamide, N-[(1S)-2-hydroxy-1-methylethyl]-4-[[[2-[[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 474798-59-9 HCAPLUS
CN 2-Pyridinecarboxamide, N-[(1R)-2-hydroxy-1-methylethyl]-4-[[[2-[[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]- (9CI) (CA INDEX NAME)

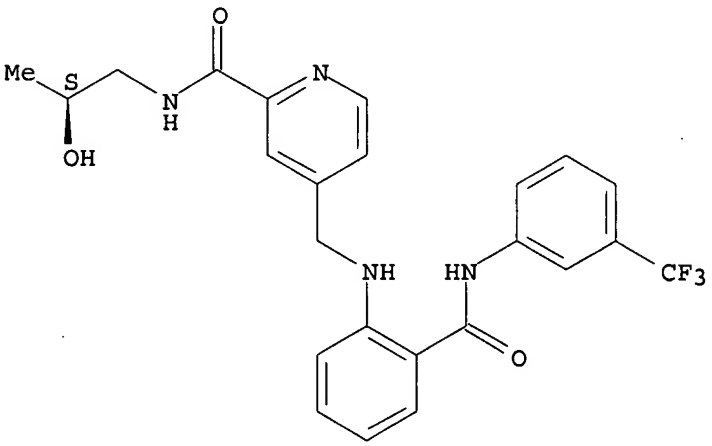
Absolute stereochemistry.



Updated Search

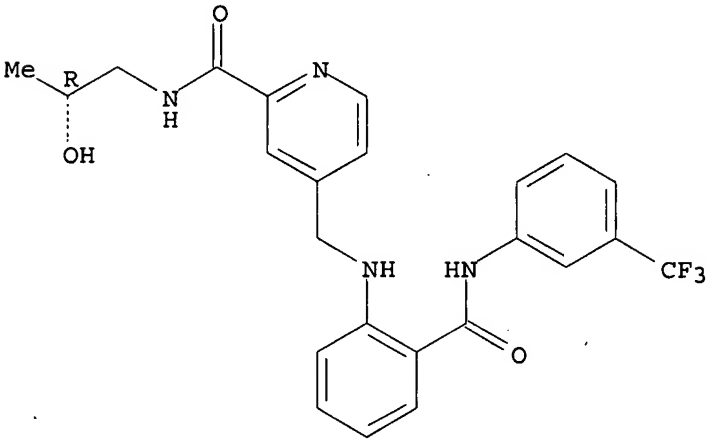
RN 474798-60-2 HCAPLUS
CN 2-Pyridinecarboxamide, N-[(2S)-2-hydroxypropyl]-4-[[[2-[[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



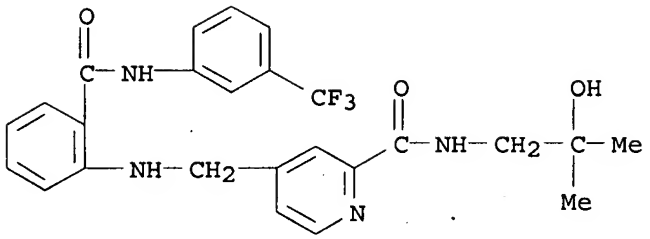
RN 474798-61-3 HCAPLUS
CN 2-Pyridinecarboxamide, N-[(2R)-2-hydroxypropyl]-4-[[[2-[[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

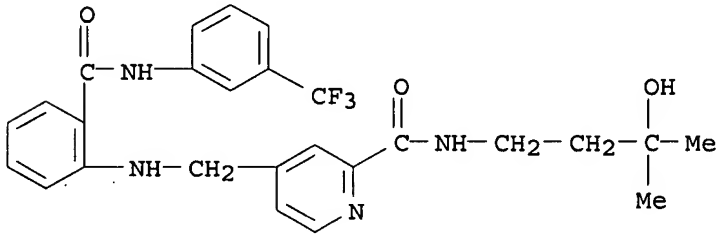


RN 474798-62-4 HCAPLUS
CN 2-Pyridinecarboxamide, N-(2-hydroxy-2-methylpropyl)-4-[[[2-[[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]- (9CI) (CA INDEX NAME)

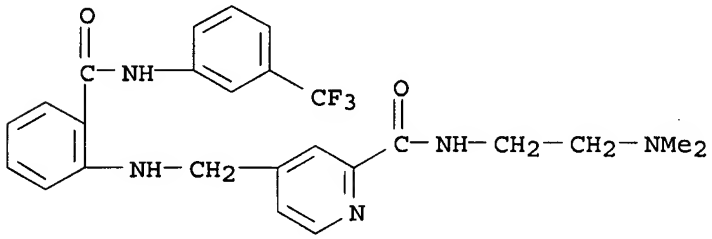
Updated Search



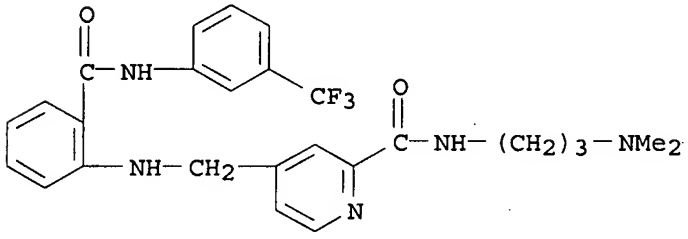
RN 474798-63-5 HCAPLUS
CN 2-Pyridinecarboxamide, N-(3-hydroxy-3-methylbutyl)-4-[[[2-[[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]- (9CI) (CA INDEX NAME)



RN 474798-64-6 HCAPLUS
CN 2-Pyridinecarboxamide, N-[2-(dimethylamino)ethyl]-4-[[[2-[[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]- (9CI) (CA INDEX NAME)



RN 474798-65-7 HCAPLUS
CN 2-Pyridinecarboxamide, N-[3-(dimethylamino)propyl]-4-[[[2-[[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]- (9CI) (CA INDEX NAME)



Updated Search

RN 474798-66-8 HCAPLUS
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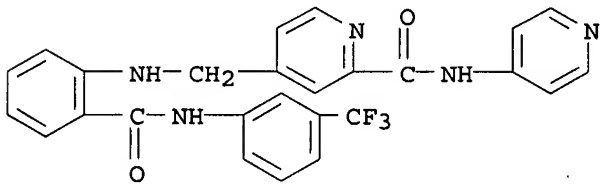
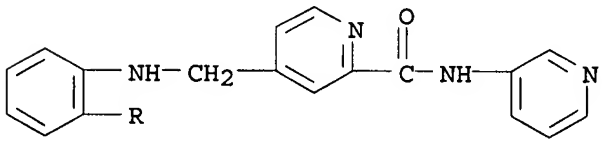
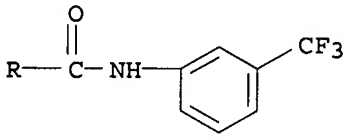
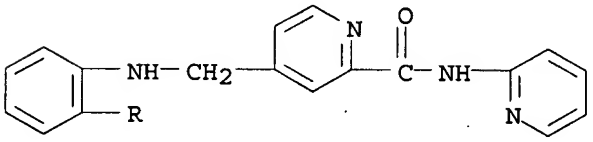


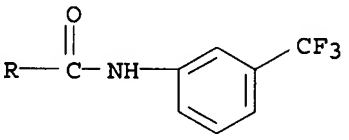
RN 474798-67-9 HCAPLUS
CN 2-Pyridinecarboxamide, N-3-pyridinyl-4-[[[2-[[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]- (9CI) (CA INDEX NAME)





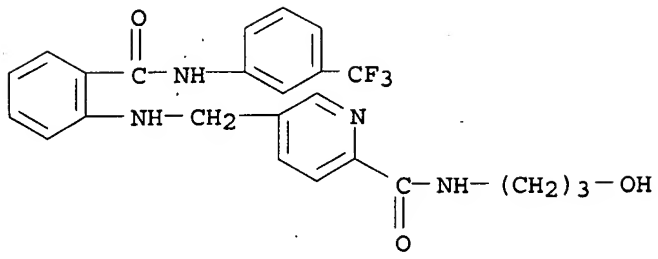
RN 474798-68-0 HCAPLUS
CN 2-Pyridinecarboxamide, N-2-pyridinyl-4-[[[2-[[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]- (9CI) (CA INDEX NAME)





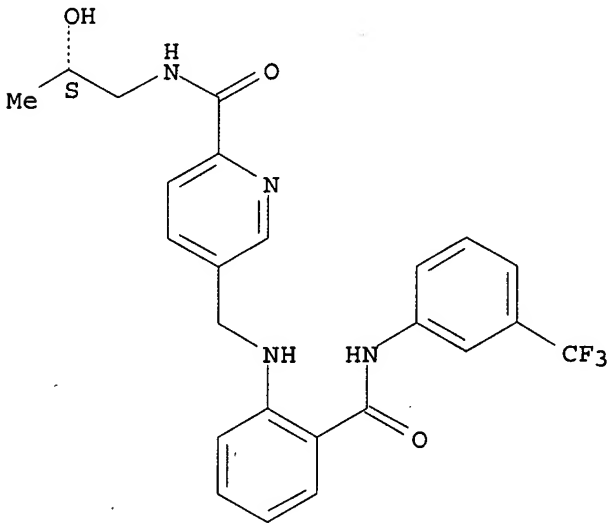
RN 474798-75-9 HCAPLUS
CN 2-Pyridinecarboxamide, N-(3-hydroxypropyl)-5-[[[2-[[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]- (9CI) (CA INDEX NAME)

Updated Search



RN 474798-76-0 HCAPLUS
CN 2-Pyridinecarboxamide, N-[(2S)-2-hydroxypropyl]-5-[[[2-[[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]- (9CI) (CA INDEX NAME)

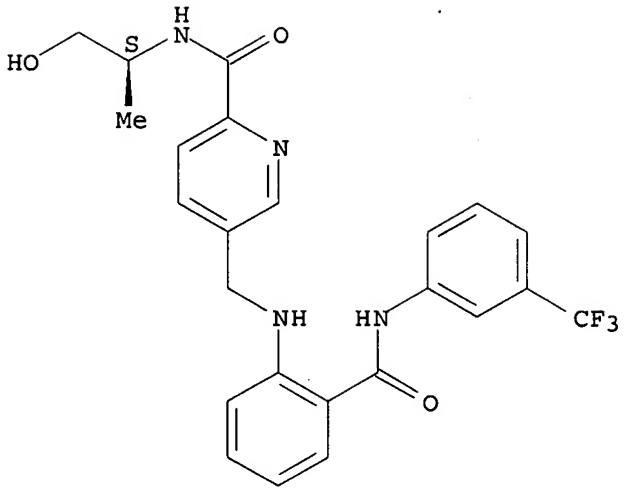
Absolute stereochemistry.



RN 474798-77-1 HCAPLUS
CN 2-Pyridinecarboxamide, N-[(1S)-2-hydroxy-1-methylethyl]-5-[[[2-[[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]- (9CI) (CA INDEX NAME)

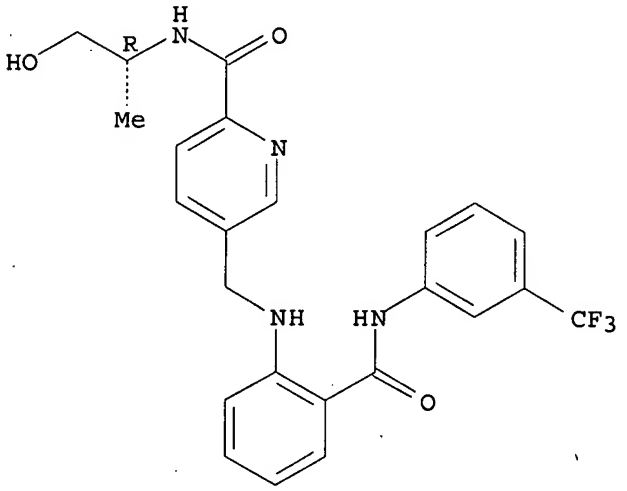
Absolute stereochemistry.

Updated Search

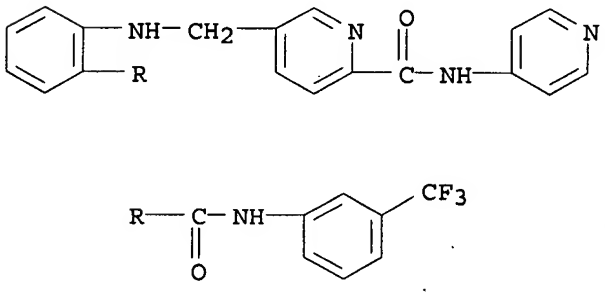


RN 474798-78-2 HCAPLUS
CN 2-Pyridinecarboxamide, N-[(1R)-2-hydroxy-1-methylethyl]-5-[[[2-[[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

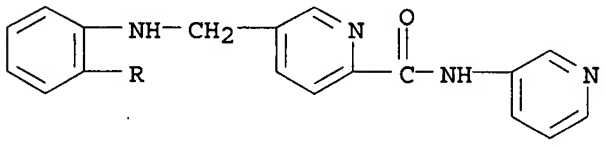


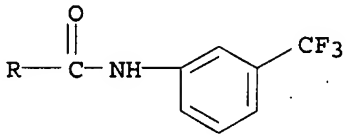
RN 474798-79-3 HCAPLUS
CN 2-Pyridinecarboxamide, N-4-pyridinyl-5-[[[2-[[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]- (9CI) (CA INDEX NAME)



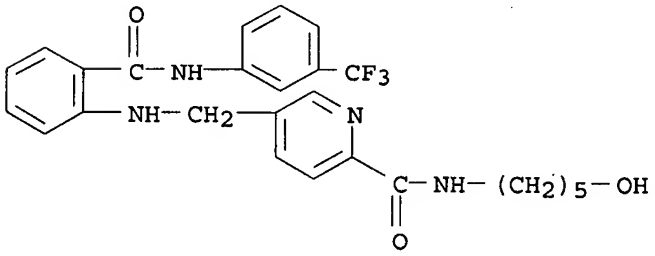
Updated Search

RN 474798-80-6 HCAPLUS
CN 2-Pyridinecarboxamide, N-3-pyridinyl-5-[[[2-[[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]- (9CI) (CA INDEX NAME)





RN 474798-81-7 HCAPLUS
CN 2-Pyridinecarboxamide, N-(5-hydroxypentyl)-5-[[[2-[[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]- (9CI) (CA INDEX NAME)



RN 474798-82-8 HCAPLUS
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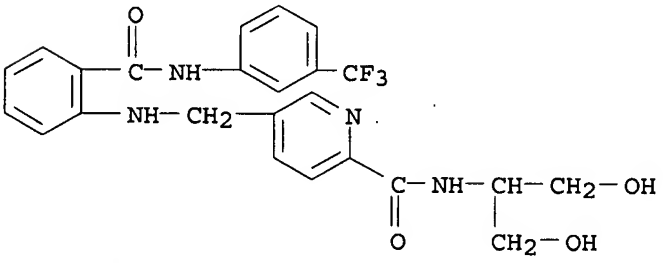

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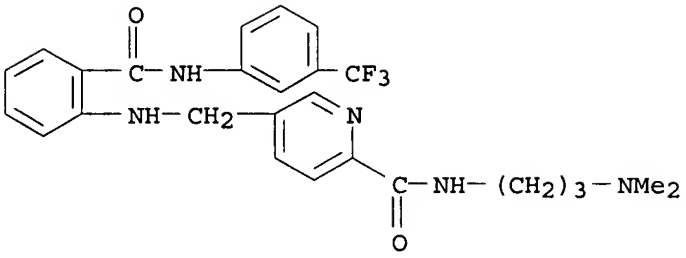
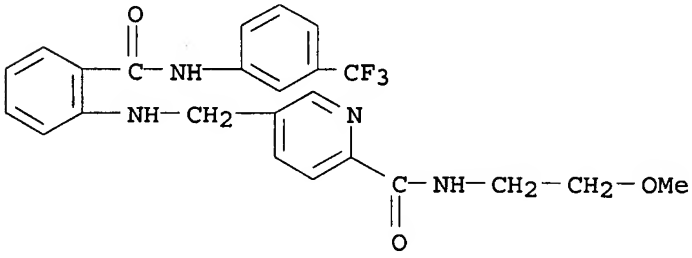
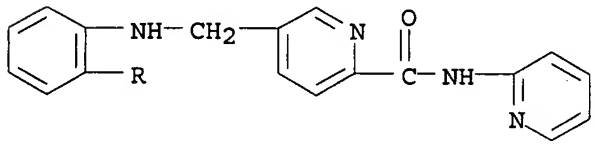
Updated Search

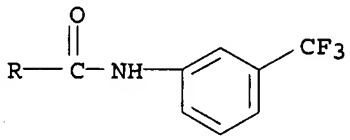


RN 474798-84-0 HCAPLUS
CN 2-Pyridinecarboxamide, N-(2-methoxyethyl)-5-[[[2-[[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]- (9CI) (CA INDEX NAME)



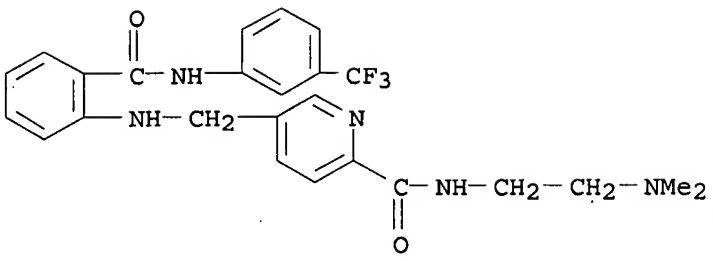
RN 474798-85-1 HCAPLUS
CN 2-Pyridinecarboxamide, N-2-pyridinyl-5-[[[2-[[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]- (9CI) (CA INDEX NAME)



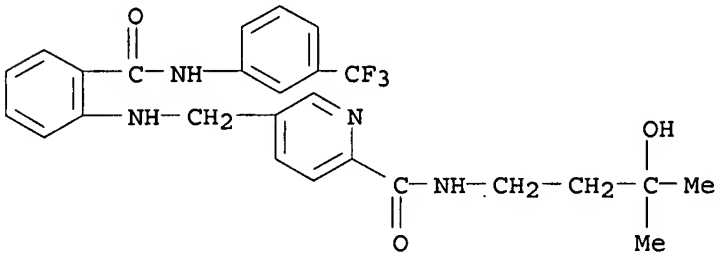


RN 474798-86-2 HCAPLUS
CN 2-Pyridinecarboxamide, N-[2-(dimethylamino)ethyl]-5-[[[2-[[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]- (9CI) (CA INDEX NAME)

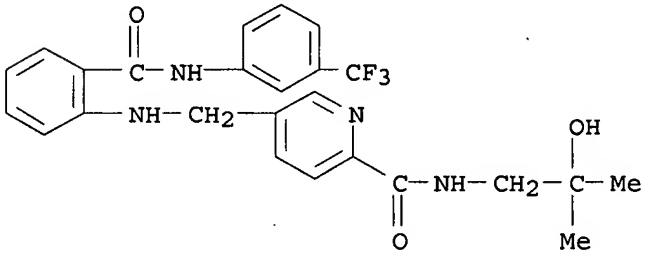
Updated Search



RN 474798-87-3 HCAPLUS
CN 2-Pyridinecarboxamide, N-(3-hydroxy-3-methylbutyl)-5-[[[2-[[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]- (9CI) (CA INDEX NAME)



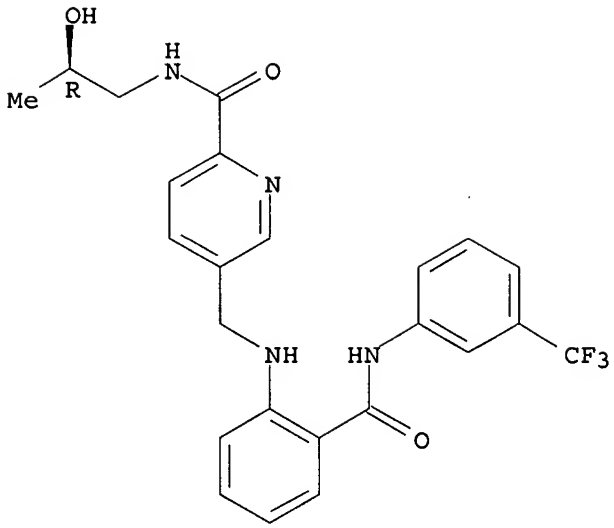
RN 474798-88-4 HCAPLUS
CN 2-Pyridinecarboxamide, N-(2-hydroxy-2-methylpropyl)-5-[[[2-[[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]- (9CI) (CA INDEX NAME)



RN 474798-89-5 HCAPLUS
CN 2-Pyridinecarboxamide, N-[(2R)-2-hydroxypropyl]-5-[[[2-[[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Updated Search



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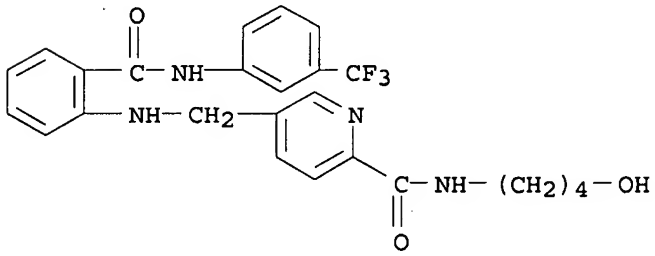
CN 2-Pyridinecarboxamide, N-(4-hydroxybutyl)-5-[[[2-[[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]- (9CI) (CA INDEX NAME)



L9 ANSWER 10 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:658116 HCAPLUS
DOCUMENT NUMBER: 137:201332
TITLE: Preparation of heterocyclylalkylamine derivatives as remedies for angiogenesis mediated diseases
INVENTOR(S): Chen, Guoqing; Adams, Jeffrey; Bemis, Jean; Booker, Shon; Cai, Guolin; Croghan, Michael; DiPietro, Lucian; Dominguez, Celia; Elbaum, Daniel; Germain, Julie; Geuns-Meyer, Stephanie; Handley, Michael; Huang, Qi; Kim, Joseph L.; Kim, Tae-seong; Kiselyov, Alexander; Ouyang, Xiaohu; Patel, Vinod F.; Smith, Leon M.; Stec, Markian; Tasker, Andrew; Xi, Ning; Xu, Shimin; Yuan, Chester Chenguang
PATENT ASSIGNEE(S): Amgen Inc., USA
SOURCE: PCT Int. Appl., 502 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

Updated Search

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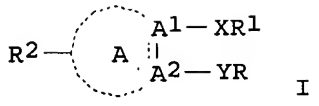
OTHER SOURCE(S):	MARPAT 137:201332				

GI

Updated Search



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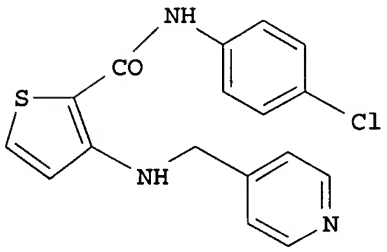


II

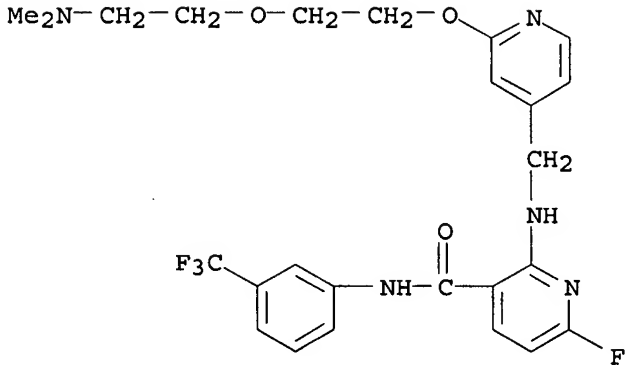
AB Title compds. [I; A1, A2 independently = C, N; A = 5-, or 6-membered partially saturated heterocyclyl, 5-, or 6-membered heterocyclyl, 9-, or 10-membered fused partially saturated heterocyclyl, 9-, 10-, or 11-membered fused heteroaryl, naphthyl, 4-, 5-, or 6-membered cycloalkenyl; X = C:ZNR3, C:ZN(R3)R4; Z = O, S; Y = N:CH, NR5(CR6R7), R8N(R5)(CR6R7), NR5(CR6R7)R8; R = 5-, or 6-membered (un)substituted heterocyclyl, 9-, 10-, 11-membered heterocyclyl; R1 = 6-10-membered (un)substituted aryl, 5-, or 6-membered (un)substituted heterocyclyl, 9-11 membered (un)substituted fused heterocyclyl, cycloalkyl, cycloalkenyl; R2 = H, halo, oxo, SH, COOH, CHO; R3 = H, alkyl, 5-, or 6-membered heterocyclyl; R4 = alkylenyl, alkenylenyl, alkynylenyl; R5 = H, alkyl, aralkyl, C6H5; R6, R7 independently = H, halo, CN, alkyl; R6R7 = cycloalkyl; R8 = alkylenyl; etc.] are prepared and are effective for prophylaxis and treatment of diseases, such as angiogenesis mediated diseases. The invention encompasses novel compds., analogs, prodrugs and pharmaceutically acceptable derivs. thereof, pharmaceutical compns. and methods for prophylaxis and treatment of diseases and other maladies or conditions involving, cancer and the like. The subject invention also relates to processes for making such compds. as well as to intermediates useful in such processes. Thus, the title compound II was prepared from Me 3-amino-2-thiophenecarboxylate, 4-chloroaniline, and 4-pyridine carboxaldehyde via coupling reaction.

IT 453563-07-0P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of heterocyclylalkylamine derivs. as remedies for angiogenesis mediated diseases)

RN 453563-07-0 HCAPLUS

CN 3-Pyridinecarboxamide, 2-[[[2-[2-[2-(dimethylamino)ethoxy]ethoxy]-4-pyridinyl]methyl]amino]-6-fluoro-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

Updated Search



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453564-71-1P 453564-76-6P 453564-80-2P
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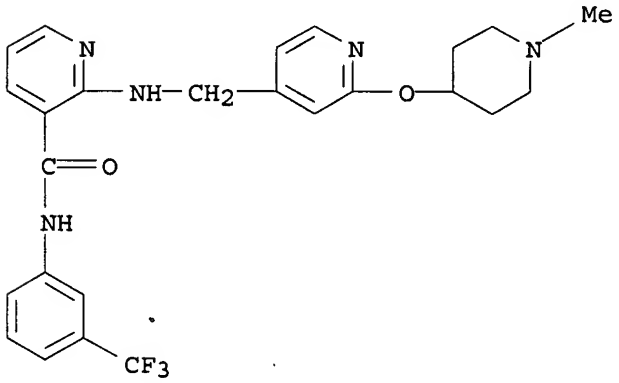
453564-92-6P 453564-93-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of heterocyclylalkylamine derivs. as remedies for angiogenesis mediated diseases)

RN 453561-97-2 HCAPLUS
CN 3-Pyridinecarboxamide, 2-[[[2-[(1-methyl-4-piperidinyl)oxy]-4-pyridinyl]methyl]amino]-N-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



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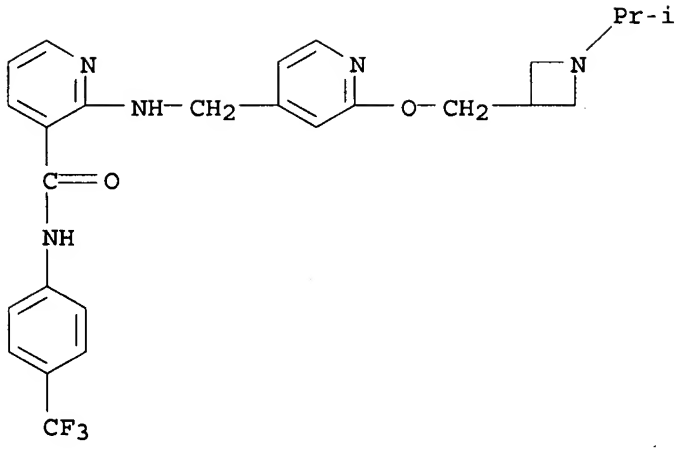
CN 3-Pyridinecarboxamide, 2-[[[2-[[1-(1-methylethyl)-3-azetidinyl]methoxy]-4-pyridinyl]methyl]amino]-N-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

Updated Search



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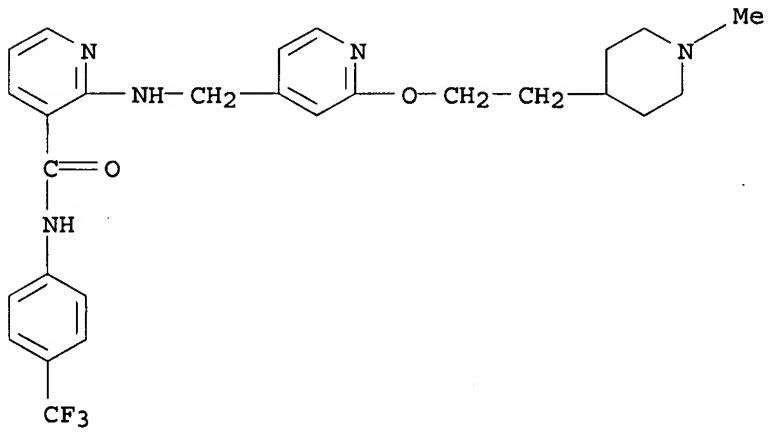

RN 453563-56-9 HCAPLUS
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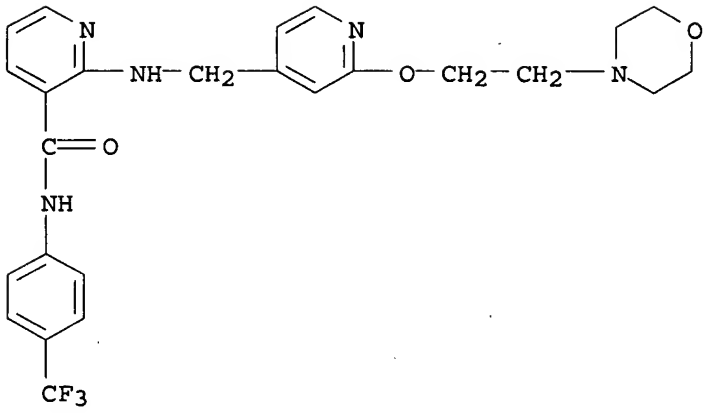
Updated Search



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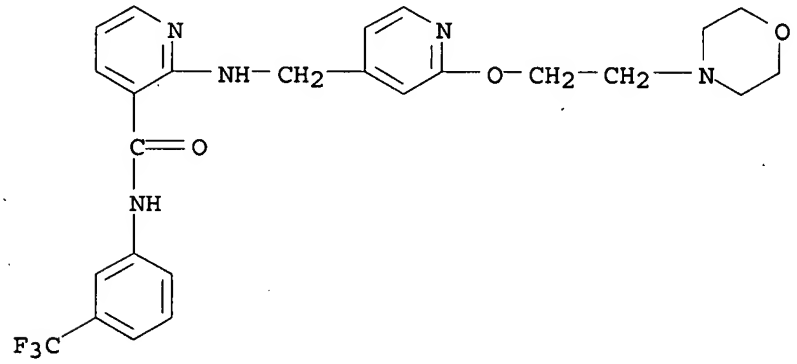
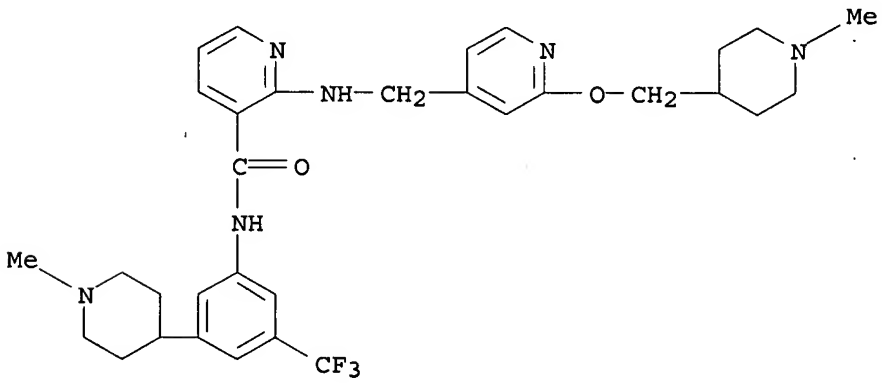


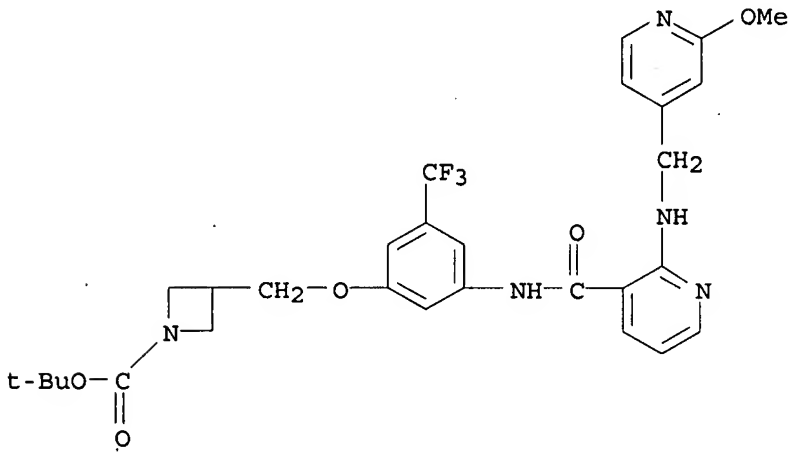
RN 453563-72-9 HCAPLUS
CN 3-Pyridinecarboxamide, 2-[[[2-[(1-methyl-4-piperidinyl)methoxy]-4-pyridinyl]methyl]amino]-N-[3-(1-methyl-4-piperidinyl)-5-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 453563-75-2 HCAPLUS

Updated Search

CN 1-Azetidinecarboxylic acid, 3-[[3-[[[2-[[(2-methoxy-4-pyridinyl)methyl]amino]-3-pyridinyl]carbonyl]amino]-5-(trifluoromethyl)phenoxy]methyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



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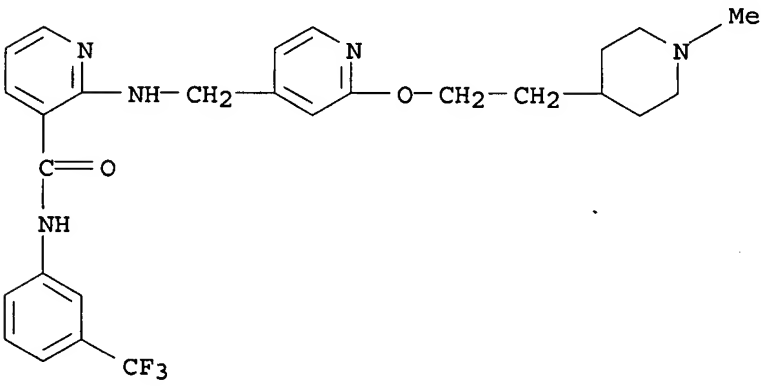

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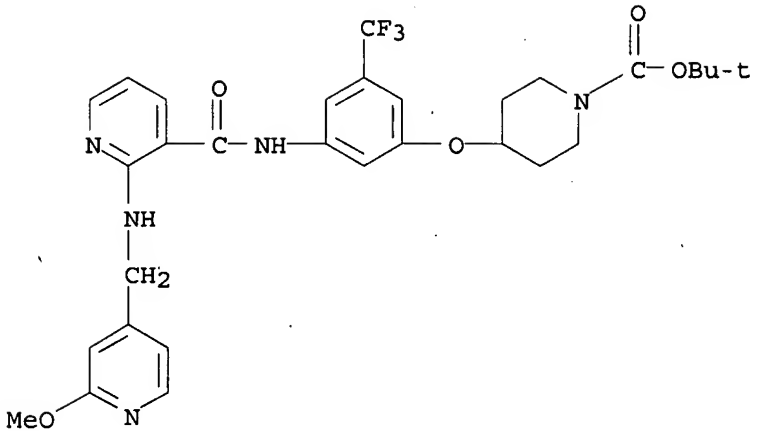
Updated Search



RN 453564-12-0 HCAPLUS
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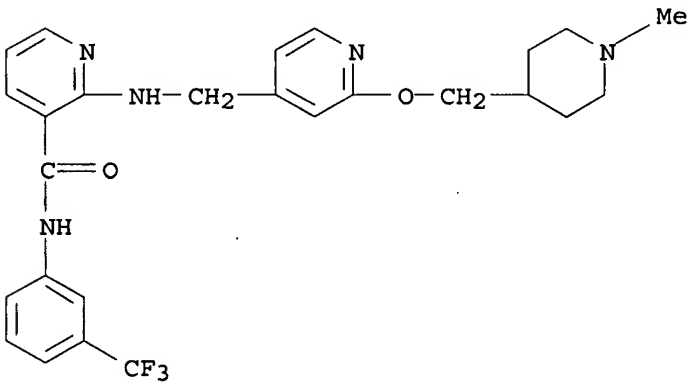

RN 453564-27-7 HCAPLUS
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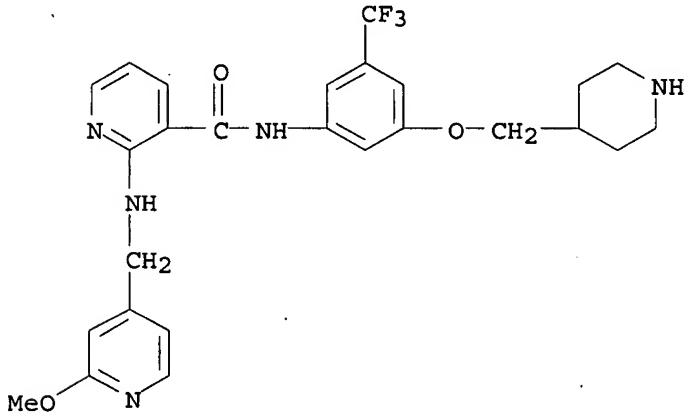

Updated Search

RN 453564-30-2 HCAPLUS
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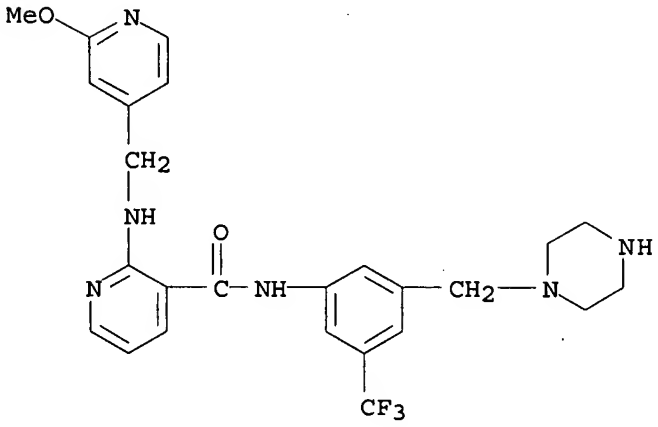

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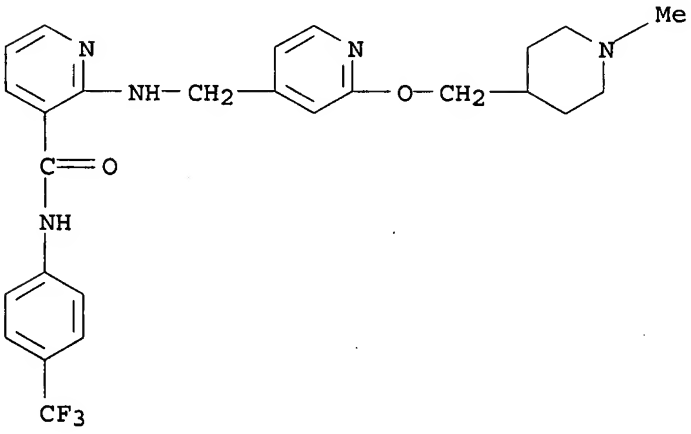
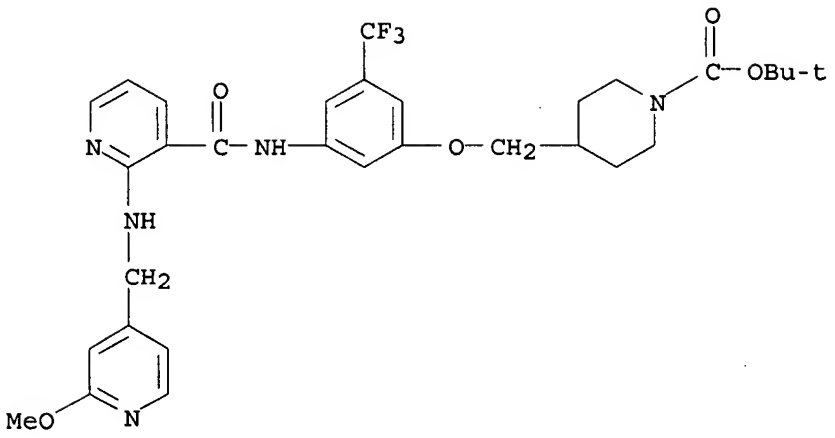
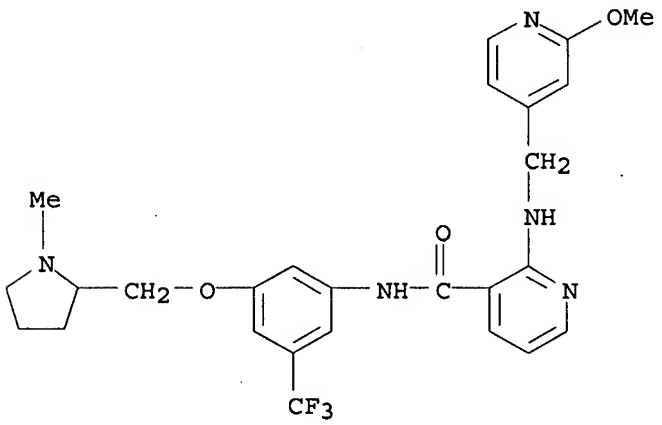


RN 453564-76-6 HCAPLUS
CN 1-Piperidinecarboxylic acid, 4-[[3-[[[2-[[(2-methoxy-4-pyridinyl)methyl]amino]-3-pyridinyl]carbonyl]amino]-5-(trifluoromethyl)phenoxy]methyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Updated Search



RN 453564-80-2 HCAPLUS
CN 3-Pyridinecarboxamide, 2-[[(2-methoxy-4-pyridinyl)methyl]amino]-N-[3-[(1-methyl-2-pyrrolidinyl)methoxy]-5-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 453564-81-3 HCAPLUS
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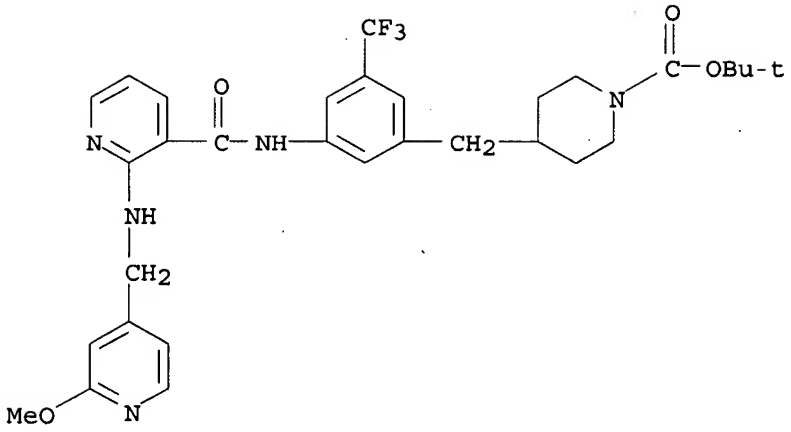
Updated Search



RN 453564-82-4 HCAPLUS
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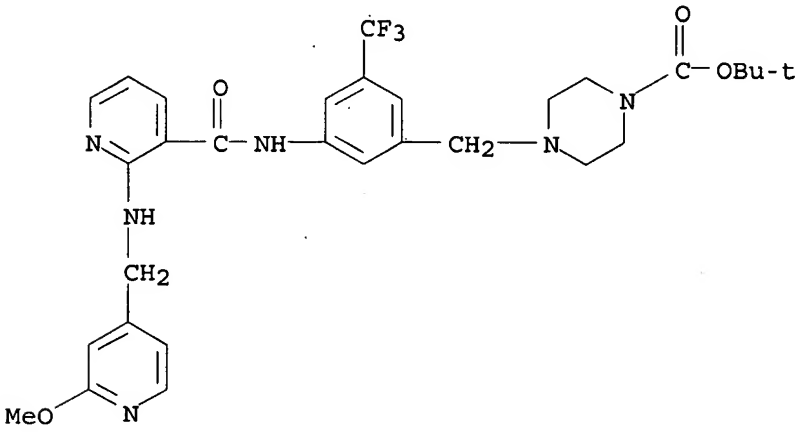

RN 453564-84-6 HCAPLUS
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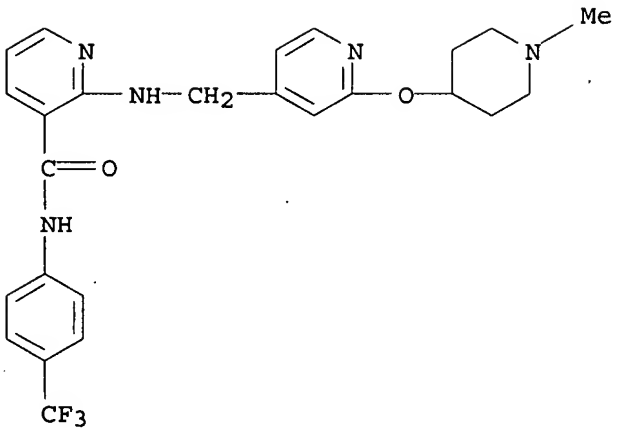
Updated Search



RN 453564-92-6 HCAPLUS
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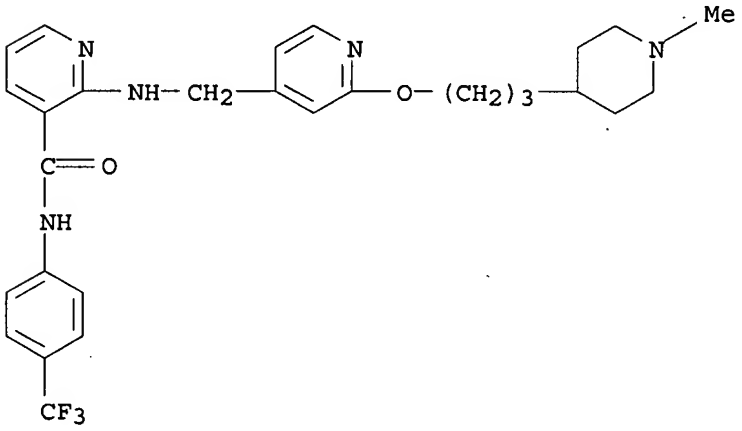

RN 453564-93-7 HCAPLUS
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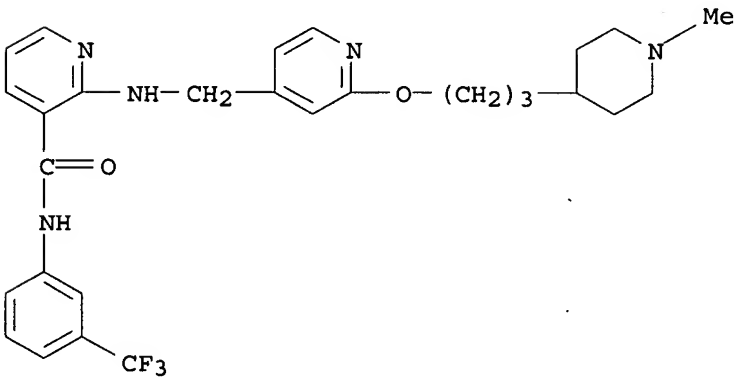

Updated Search

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REFERENCE COUNT:          19    THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS
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FULL ESTIMATED COST                                      89.52     265.88

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)            SINCE FILE      TOTAL
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CA SUBSCRIBER PRICE                                     -12.48     -12.48

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FILE COVERS 1907-1966
FILE LAST UPDATED:  01 May 1997 (19970501/UP)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.  Title keywords, authors, patent
  assignees, and patent information, e.g., patent numbers, are
  now searchable from 1907-1966.  TIFF images of CA abstracts
  printed between 1907-1966 are available in the PAGE
  display formats.

  New CAS Information Use Policies, enter HELP USAGETERMS for details.

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FILE COVERS 1907 - 1 Oct 2007 VOL 147 ISS 15
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New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L12 ANSWER 1 OF 16 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:538988 HCAPLUS
DOCUMENT NUMBER: 145:46079
TITLE: Preparation of bicyclic amides as kinase inhibitors
INVENTOR(S): Bold, Guido; Capraro, Hans-Georg; Caravatti, Giorgio; Floersheimer, Andreas; Furet, Pascal ; Manley, Paul W.; Vaupel, Andrea; Pissot Soldermann, Carole; Gessier, Francois; Schnell, Christian; Littlewood-Evans, Amanda Jane; Kapa, Prasad Koteswara; Bajwa, Joginder S.; Jiang, Xinglong
PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis Pharma G.M.B.H.
SOURCE: PCT Int. Appl., 109 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006059234	A2	20060608	WO 2005-IB4030	20050914
WO 2006059234	A3	20060720		

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Updated Search

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NO 2007001875	A	20070614	NO 2007-1875		20070413
PRIORITY APPLN. INFO.:			GB 2004-20520	A	20040915
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			WO 2005-IB4030	W	20050914

OTHER SOURCE(S): MARPAT 145:46079
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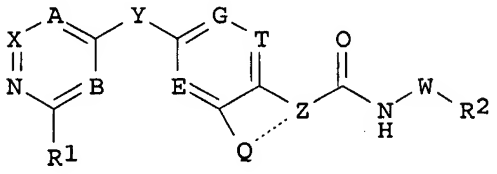

I

AB The invention relates to compds. I [R1 = H, halo, CN, etc.; R2 = substituted cycloalkyl, aryl, heterocyclyl; A, B and X = CR7 or N; E, G and T = CR8 or N; R7, R8 = H, halo, (un)substituted alkyl; Y = O, S, CH2, etc.; Z = CH or N and Q = (un)substituted alkylene or alkenylene (wherein one or more of the carbon atoms may be replaced by a heteroatom selected from N, O or S; and the bond between Q and Z is a single bond; with the proviso that if Z = N, Q is not unsubstituted unbranched alkylene); or Z = C and Q is as defined above wherein the bond between Q and Z characterized by a dotted line is a double bond; W is either not present or alkylene] and their use in the treatment of the animal or human body, to pharmaceutical compns. comprising a compound I and to the use of a compound I for the preparation of pharmaceutical compns. for use in the treatment of protein kinase dependent diseases, especially of proliferative diseases, such as in particular tumor diseases. Over 100 compds. I were prepared E.g., a 3-step synthesis of rac-5-(2-amino-6-chloropyrimidin-4-yloxy)-4-fluoro-2-methyl-2,3-dihydroindole-1-carboxylic acid (3-trifluoromethylphenyl)amide, starting from 2-amino-4,6-dichloropyrimidine and 4-fluoro-5-hydroxy-2-methylindole, was given.

L12 ANSWER 2 OF 16 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:318488 HCAPLUS
DOCUMENT NUMBER: 144:369909
TITLE: Preparation of cyclic diaryl ureas suitable as tyrosine kinase inhibitors
INVENTOR(S): Bold, Guido; Caravatti, Giorgio; Floersheimer, Andreas; Furet, Pascal;

Updated Search

	Manley, Paul W.; Pissot Soldermann, Carole; Vaupel, Andrea
PATENT ASSIGNEE(S):	Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SOURCE:	PCT Int. Appl., 140 pp.
	CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

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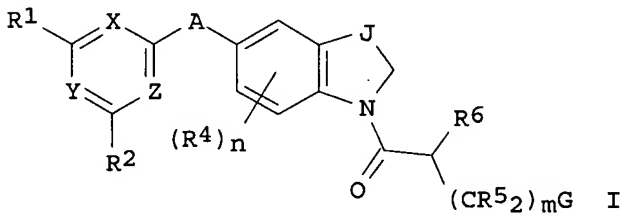
IN 2007DN01701	A	20070817	IN 2007-DN1701		20070302
PRIORITY APPLN. INFO.:			GB 2004-21525	A	20040928
			WO 2005-EP10408	W	20050927

OTHER SOURCE(S): CASREACT 144:369909; MARPAT 144:369909

GI



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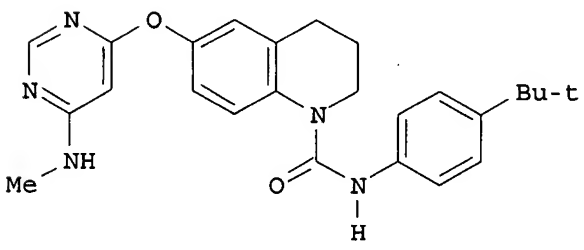


II

Updated Search

AB Title compds. I [A = S, O, CH2, etc.; X, Y and Z independently = N or CR3 wherein at least two of X, Y and Z = N; R1-3 independently = halo, OH, alkyl, etc.; R4 = halo, OH, alkyl, mercapto, etc.; R5-7 independently = H or alkyl; G = CN or (un)substituted 5-6 membered monocyclic or 8-12 membered bicyclic or tricyclic ring which may contain 0-3 heteroatoms and be optionally saturated or unsatd.; J = (CR72)p; wherein m, n or p independently = 0-3] and their pharmaceutically acceptable salts, esters, N-oxides or prodrugs thereof are prepared and disclosed for the use in the treatment of protein kinase dependent diseases. Thus, e.g., II was prepared by reaction of 6-methylamino-4-(1,2,3,4-tetrahydroquinolin-6-yloxy)pyrimidine (preparation given) with 4-tert-butylphenylisocyanate. Assays are described for determining activity of I as kinase inhibitors (no data). Specific tyrosine kinases identified as associated with a proliferative condition include ras, Abl, VEGF-receptor tyrosine kinase, Flt3, Bcr-Abl receptors, and substitution mutants of Bcr-Abl. Further disclosed are claims to the use of I in the manufacture of pharmaceutical compns. for use in the treatment of said diseases, methods of use of diaryl urea derivs. in the treatment of said diseases, pharmaceutical prepns. comprising these novel diaryl urea derivs., processes for the manufacture of the novel diaryl urea derivs., the use or methods of use of the novel diaryl urea derivs. as mentioned above, and/or these novel diaryl urea derivs. for use in the treatment of the animal or human body.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 3 OF 16 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:15086 HCAPLUS

DOCUMENT NUMBER: 144:108347

TITLE: Preparation of pyrimidine urea derivatives as kinase inhibitors for use against proliferative diseases

INVENTOR(S): Ding, Qiang; Gray, Nathanael Schiander; Li, Bing; Liu, Yi; Sim, Taebo; Uno, Tetsuo; Zhang, Guobao; Pissot Soldermann, Carole; Breitenstein, Werner; Bold, Guido; Caravatti, Giorgio; Furet, Pascal ; Guagnano, Vito; Lang, Marc; Manley, Paul W. ; Schoepfer, Joseph; Spanka, Carsten

PATENT ASSIGNEE(S): Novartis AG, Switz.

SOURCE: PCT Int. Appl., 327 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

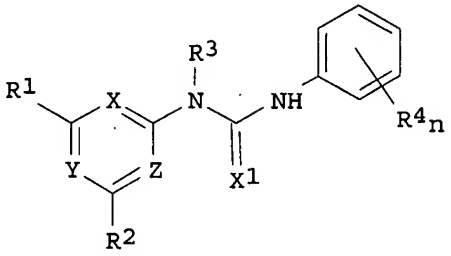
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006000420	A1	20060105	WO 2005-EP6815	20050623
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2005256491	A1	20060105	AU 2005-256491	20050623
CA 2570873	A1	20060105	CA 2005-2570873	20050623

Updated Search

EP 1761505 A1 20070314 EP 2005-756693 20050623
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, HR, LV
CN 101035769 A 20070912 CN 2005-80024896 20050623
IN 2006DN06843 A 20070831 IN 2006-DN6843 20061116
NO 2007000432 A 20070326 NO 2007-432 20070123
PRIORITY APPLN. INFO.: US 2004-582425P P 20040624
GB 2005-12324 A 20050616
WO 2005-EP6815 W 20050623
OTHER SOURCE(S): MARPAT 144:108347
GI



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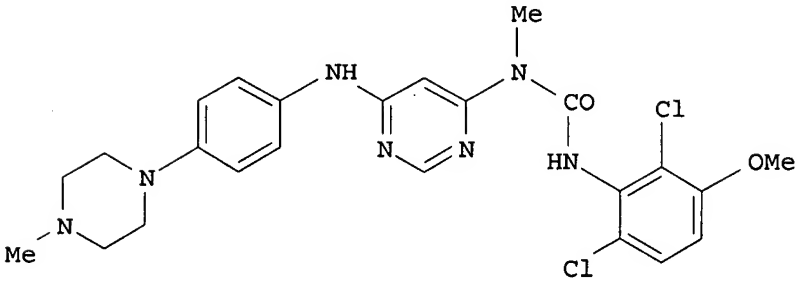

II

AB The invention relates to pyrimidine urea derivs. (shown as I; variables defined below; e.g. 3-(2,6-dichloro-3-methoxyphenyl)-1-methyl-1-[6-[[4-(4-methylpiperazin-1-yl)phenyl]amino]pyrimidin-4-yl]urea (II)), to processes for the preparation of these compds., pharmaceutical compns. containing same, the use thereof optionally in combination with ≥1 other pharmaceutically active compds. for the therapy of a disease which responds to an inhibition of protein kinase activity, and a method for the treatment of such a disease. Inhibitory activity of some examples of I are included, e.g. N-[3-[3-(6-aminopyrimidin-4-yl)-3-[3-(2-oxopyrrolidin-1-yl)propyl]ureido]-4-methylphenyl]-3-trifluoromethylbenzamide at a concentration of 10 μM inhibits the following kinases by the percentage shown in brackets: wild-type Abl (99%), c-RAF (99%), CSK (97%), c-SRC (100%), FGFR35 (99%), JNK2α2 (93%), lck (100%), MKK6 (88%), p70S6K (81%), ROS (95%), SAPK2α (99%), SAPK2β (99%), Tie2 (100%) and TrkB (99%). For I: n = 0-5; X, Y and Z = N or CR5, wherein at least two of X, Y and Z are N; X1 is O; R1, R2, R3 and R4, if present, = an organic or inorg. moiety, where the inorg. moiety especially = halo, especially chloro, hydroxy, cyano, azido, nitro; and where the organic moiety is (un)substituted and may be attached via a linker, -L1-, the organic moiety especially = H lower aliphatic, amino, guanidino, hydroxyguanidino, formamidino, isothioureido, et al. and -L1-

Updated Search

has 1-5 in-chain atoms (e.g. = C, N, O and S) and optionally = (i) C1-C4 alkyl, such an alkyl group optionally being interrupted and/ or terminated by an -O-, -C(O)- or -NRa- linkage, -O-, -S-, -C(O)-, cyclopropyl (regarded as having two in-chain atoms) and chemical appropriate combinations thereof. R1 can also = -X5NR7R8, -X5NR7X5NR7R8, -X5NR7X5C(O)OR8, -X5OR7, -X5R7 and -X5S(O)0-2R7 (X5 is a bond or (un)substituted C1-4alkylene; R7 = H, C1-6alkyl, C6-10aryl-C0-4alkyl, C5-10heteroaryl-C0-4alkyl, C3-10cycloalkyl-C0-4alkyl and C3-10heterocycloalkyl-C0-4alkyl; and R8 = H and C1-6alkyl; or R7 and R8 together with the N to which R7 and R8 are both attached form heteroaryl or heterocycloalkyl); wherein R3 can alternatively = H, C1-4alkyl, C6-10aryl-C0-4alkyl, C5-10 heteroaryl-C0-4alkyl, C3-10cycloalkyl-C0-4alkyl and C3-10heterocycloalkyl-C0-4alkyl. Each R4 is the same or different and = an organic or inorg. moiety, e.g. halogen, hydroxy, protected hydroxy; one of the R4 can also = -L1-A-R16m (L1 is a linker; m is 0-5; A is a ring; R16, if present, = an organic or inorg. moiety, where the inorg. moiety especially = halo, especially chloro, hydroxy, cyano, azido, nitro; and where the organic moiety is (un)substituted and may be attached via a linker, -L2-, the organic moiety being especially = H, lower aliphatic (especially C1-C4 aliphatic), et al.; L1 and L2 each independently = moieties having 1-5 in-chain atoms (e.g. = C, N, O and S) and optionally being = C1-C4 alkyl, such an alkyl group optionally being interrupted and/or terminated by an -O-, -C(O)- or -NRa- linkage, -O-, -S-, -C(O)-, cyclopropyl (regarded as having two in-chain atoms) and chemical appropriate combinations thereof); addnl. details including provisos are given in the claims. Although the methods of preparation are not claimed, prepns. and/or characterization data for >200 examples of I are included. For example, II was prepared from 2,6-dichloro-3-methoxyphenyl isocyanate (preparation given) and N-methyl-N'-[4-(4-methylpiperazin-1-yl)phenyl]pyrimidine-4,6-diamine (preparation given).

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 4 OF 16 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:515506 HCAPLUS
DOCUMENT NUMBER: 141:71453
TITLE: Preparation of anthranilic acid amide derivatives as neoplastic inhibitors
INVENTOR(S): Bold, Guido; Furet, Pascal; Manley, Paul William
PATENT ASSIGNEE(S): Novartis Ag, Switz.; Novartis Pharma GmbH
SOURCE: PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004052884	A1	20040624	WO 2003-EP14086	20031211

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SE, SG, SK, SY, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW

RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE,

Updated Search

DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR

CA 2506164	A1	20040624	CA 2003-2506164	20031211
AU 2003294834	A1	20040630	AU 2003-294834	20031211
EP 1572686	A1	20050914	EP 2003-785795	20031211
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003017292	A	20051108	BR 2003-17292	20031211
CN 1720244	A	20060111	CN 2003-80104845	20031211
JP 2006511518	T	20060406	JP 2004-558075	20031211
US 2006128684	A1	20060615	US 2005-538199	20050609
PRIORITY APPLN. INFO.:			GB 2002-29022 A	20021212
			WO 2003-EP14086 W	20031211

OTHER SOURCE(S): MARPAT 141:71453

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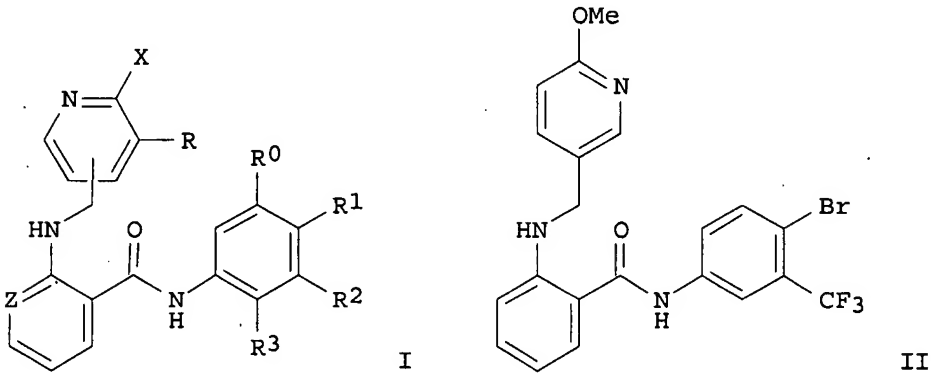


I II

AB The title compds. I [wherein R and R0 = independently H, halo, (un)substituted alkyl, alkenyl, alkynyl, aryl, heteroaryl, etc.; R1 = H, halo, (un)substituted alkyl, alkenyl, alkynyl, alkoxy, OCF3, OCH2CF3, OCH2CH2CF3, or OCH2CH2CH2CF3; R2 = perfluoroalkyl; R3 = H or halo; X = OH, alkoxy, alkylthio, imino, alkylimino, halo, etc.; Z = N or CH] or salts, N-oxides, or tautomers thereof are prepared as neoplastic inhibitors for the treatment of human or animal body. For example, the compound II was prepared in a multi-step synthesis. Formulations containing I as an active ingredient were also described.

L12 ANSWER 5 OF 16 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	2004:216609 HCAPLUS
DOCUMENT NUMBER:	140:417028
TITLE:	Advances in the structural biology, design and clinical development of VEGF-R kinase inhibitors for the treatment of angiogenesis
AUTHOR(S):	Manley, Paul William; Bold, Guido; Brueggen, Josef; Fendrich, Gabrielle; Furet, Pascal; Mestan, Jurgen; Schnell, Christian; Stolz, Barbara; Meyer, Thomas; Meyhack, Bernd; Stark, Wilhelm; Strauss, Andre; Wood, Jeanette
CORPORATE SOURCE:	Novartis Institutes of Biomedical Research, Basel, CH-4002, Switz.
SOURCE:	Biochimica et Biophysica Acta, Proteins and Proteomics (2004), 1697(1-2), 17-27 CODEN: BBAPBW; ISSN: 1570-9639
PUBLISHER:	Elsevier B.V.
DOCUMENT TYPE:	Journal; General Review

Updated Search

LANGUAGE: English

AB A review. Initial studies with angiogenesis inhibitors showed little clin. benefit. However, recently reported clin. studies in colorectal cancer have shown that bevacizumab, a vascular endothelial growth factor (VEGF) monoclonal antibody, in combination with cytotoxic therapy has pos. effects on patient survival. Furthermore, the VEGF receptor kinase (VEGF-R) tyrosine kinase inhibitor, vatalanib, has also shown encouraging results in colorectal cancer, with mol. resonance imaging providing evidence that the anti-tumor efficacy was indeed the result of anti-angiogenic activity. Both of these agents are progressing in phase III trials. This proof of concept has stimulated the desire for second-generation VEGF-R inhibitors having an improved profile. Structural biol. insight regarding the binding mode of protein kinase inhibitors is valuable for the design of mols. possessing superior selectivity, efficacy and tolerability. Towards this goal, the authors have developed a new series of VEGF-R2 kinase inhibitors, based upon an anthranilic acid amide scaffold. An x-ray crystal structure of a representative compound, AAL993 (ZK260253), in complex with the catalytic domain of diphosphorylated VEGF-R2 has revealed that this mol. binds to an inactive conformation of the protein. This binding mode, similar to that observed for the anti-leukemia drug, imatinib in complex with c-Abl kinase, may be responsible for the high selectivity of AAL993 and provides valuable insight for the design of further compds.

REFERENCE COUNT: 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 6 OF 16 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:950982 HCAPLUS

DOCUMENT NUMBER: 140:16736

TITLE: Preparation of diarylurea derivatives useful for the treatment of protein kinase dependent diseases

INVENTOR(S): Floersheimer, Andreas; Furet, Pascal; Manley, Paul William; Bold, Guido; Boss, Eugen; Guagnano, Vito; Vaupel, Andrea

PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.

SOURCE: PCT Int. Appl., 170 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

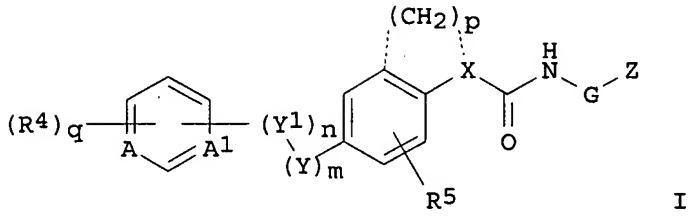
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003099771	A2	20031204	WO 2003-EP5634	20030528
WO 2003099771	A3	20040401		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SE, SG, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW				
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR				
CA 2484288	A1	20031204	CA 2003-2484288	20030528
AU 2003242591	A1	20031212	AU 2003-242591	20030528
AU 2003242591	B2	20070726		
BR 2003011313	A	20050215	BR 2003-11313	20030528
EP 1511730	A2	20050309	EP 2003-755147	20030528
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

Updated Search

CN 1656073	A	20050817	CN 2003-812280		20030528
JP 2005527622	T	20050915	JP 2004-507429		20030528
ZA 2004008314	A	20060726	ZA 2004-8314		20041014
IN 2004CN02670	A	20070720	IN 2004-CN2670		20041125
MX 2004PA11789	A	20050331	MX 2004-PA11789		20041126
NO 2004005521	A	20041217	NO 2004-5521		20041217
US 2006128734	A1	20060615	US 2005-515113		20051208
PRIORITY APPLN. INFO.:			GB 2002-12413	A	20020529
			GB 2003-5684	A	20030312
			GB 2003-9219	A	20030423
			WO 2003-EP5634	W	20030528

OTHER SOURCE(S): MARPAT 140:16736
GI



I

AB The invention relates to the use of diaryl urea derivs. [I; G is not present and Z = a radical of the formula Q; A = CH, N, N→O; A1 = N, N→O, with the proviso that not more than one of A and A1 can be N→O; n = 1, 2; m = 0-2; p = 0, 2, 3; q = 0-5; X = (un)substituted NH if p = 0; or if p is 2 or 3, X = nitrogen which together with (CH2)p and the bonds represented in dotted (interrupted) lines (including the atoms to which they are bound) forms a ring, or X = CHK (wherein K = H or lower alkyl) and p = 0, with the proviso that the bonds represented in dotted lines, if p = 0, are absent; Y1 = O, S, CH2; Y2 = O, S, NH; with the proviso that (Y1)n-(Y2)m does not include O-O, S-S, NH-O, NH-S or S-O groups; R1, R2, R3, R5 = independently H or an inorg. or organic moiety or any two of them together form a lower alkylenedioxy bridge bound via the oxygen atoms, and the remaining one of these moieties is hydrogen or an inorg. or organic moiety; R4 (if present, i.e., if q is not zero) is an inorg. or organic moiety] or tautomers thereof or pharmaceutically acceptable salts thereof in the treatment of protein kinase dependent diseases or for the manufacture of pharmaceutical compns. for use in the treatment of said diseases, especially a proliferative disease depending on any one or more of the following (tyrosine) protein kinases such as ras, Abl, VEGF-receptor tyrosine kinase, Flt3, and/or Bcr-Abl activity. Also disclosed are the use of the compds. I for the manufacture of pharmaceutical compns. for use in the treatment of said diseases, methods of use of the compds. I in the treatment of said diseases, pharmaceutical prepns. comprising the compds. I for the treatment of said diseases, processes for the manufacture of the compds. I, the use or methods of use of the compds. I as mentioned above, and/or the compds. I for use in the treatment of the animal or human body. For example, N-(4-(pyridin-4-yloxy)phenyl)-N'-(4-2,2,2-trifluoroethoxy-3-trifluoromethylphenyl)urea and N-[4-[6-(4-hydroxyphenylamino)pyrimidin-4-yl]phenyl]-N'-(4-2,2,2-trifluoroethoxy-3-trifluoromethylphenyl)urea at 10 μM inhibited gene c-Abl protein kinase by 98%, Kdr receptor tyrosine kinase by 100 and 96%, resp., and Flt3 receptor tyrosine kinase by 100%.

L12 ANSWER 7 OF 16 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:665525 HCAPLUS

Updated Search

DOCUMENT NUMBER: 139:345320
TITLE: Identification of a new chemical class of potent angiogenesis inhibitors based on conformational considerations and database searching
AUTHOR(S): Furet, Pascal; Bold, Guido; Hofmann, Francesco; Manley, Paul; Meyer, Thomas; Altmann, Karl-Heinz
CORPORATE SOURCE: Oncology Research, Novartis Pharma AG, Basel, CH-4002, Switz.
SOURCE: Bioorganic & Medicinal Chemistry Letters (2003), 13(18), 2967-2971
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:345320

AB The vascular endothelial growth factor (VEGF) tyrosine kinase receptors KDR and Flt-1 are targets of current interest in anticancer drug research. PTK787/ZK222584 is a potent inhibitor of these enzymes in clin. evaluation as an antiangiogenic agent. The development of a hypothesis concerning the bioactive conformation of this compound has led to the discovery of a new class of potent inhibitors of KDR and Flt-1, the anthranilamides. This could be achieved with a limited exptl. effort, which only involved the testing of one archive compound and the synthesis and testing of one appropriate analog.

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

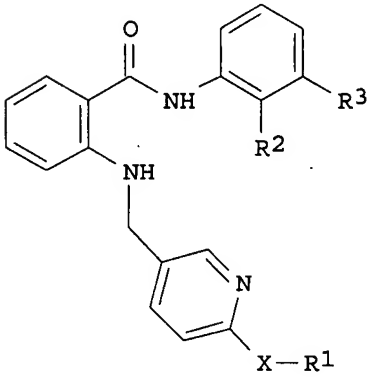
L12 ANSWER 8 OF 16 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:376825 HCAPLUS
DOCUMENT NUMBER: 138:385308
TITLE: Preparation of anthranilic acid amides and their use as vascular endothelial growth factor receptor tyrosine kinase inhibitors
INVENTOR(S): Bold, Guido; Furet, Pascal; Manley, Paul William
PATENT ASSIGNEE(S): Novartis AG, Switz.; Novartis Pharma Gmbh
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003040102	A1	20030515	WO 2002-EP12444	20021107
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NO, NZ, OM, PH, PL, PT, RO, RU, SE, SG, SI, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR				
TW 260222	B	20060821	TW 2002-91132669	20021106
CA 2463968	A1	20030515	CA 2002-2463968	20021107
AU 2002351909	A1	20030519	AU 2002-351909	20021107
AU 2002351909	B2	20070426		
EP 1446382	A1	20040818	EP 2002-787595	20021107
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				

Updated Search

BR 2002013970	A	20040831	BR 2002-13970		20021107
CN 1585750	A	20050223	CN 2002-822209		20021107
JP 2005511602	T	20050428	JP 2003-542148		20021107
NZ 532590	A	20051223	NZ 2002-532590		20021107
ZA 2004002940	A	20050210	ZA 2004-2940		20040419
US 2005096356	A1	20050505	US 2004-494591		20040505
US 7091224	B2	20060815			
IN 2004CN00972	A	20060203	IN 2004-CN972		20040506
NO 2004002187	A	20040526	NO 2004-2187		20040526
US 2006178409	A1	20060810	US 2006-374720		20060314
PRIORITY APPLN. INFO.:			GB 2001-26902	A	20011108
			WO 2002-EP12444	W	20021107
			US 2004-494591	A1	20040505

OTHER SOURCE(S): MARPAT 138:385308
GI



I

AB Anthranilic acid amide derivs. [I; R1, R2 = H, lower alkyl; R3 = lower perfluoroalkyl; X = O, S; e.g., 2-[(6-Methoxy-3-pyridinyl)methyl]amino-N-[3-(trifluoromethyl)phenyl]benzamide hydrochloride, m.p. 133-135°], which are vascular endothelial growth factor receptor tyrosine kinase inhibitors for the treatment of neoplastic disease, of retinopathy or age-related macular degeneration, are prepared and a I-containing formulation presented (e.g., a soft capsule).

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 9 OF 16 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:376824 HCAPLUS
DOCUMENT NUMBER: 138:368777
TITLE: Preparation of pyridyl-substituted anthranilic acid amides for treating neoplastic disease
INVENTOR(S): Bold, Guido; Furet, Pascal; Manley, Paul William
PATENT ASSIGNEE(S): Novartis AG, Switz.; Novartis Pharma Gmbh
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

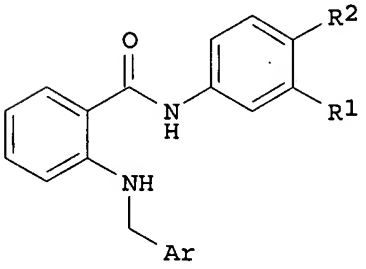
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

Updated Search

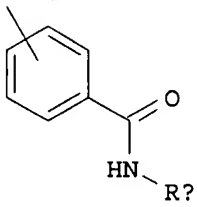
WO 2003040101	A1	20030515	WO 2002-EP12445		20021107
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SE, SG, SI, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW					
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR					
TW 260985	B	20060901	TW 2002-91132668		20021106
CA 2462390	A1	20030515	CA 2002-2462390		20021107
AU 2002342889	A1	20030519	AU 2002-342889		20021107
AU 2002342889	B2	20070301			
EP 1446381	A1	20040818	EP 2002-779536		20021107
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK					
BR 2002013939	A	20040831	BR 2002-13939		20021107
CN 1578768	A	20050209	CN 2002-821430		20021107
JP 2005508382	T	20050331	JP 2003-542147		20021107
NZ 532587	A	20060224	NZ 2002-532587		20021107
NZ 543915	A	20070629	NZ 2002-543915		20021107
US 2004248947	A1	20041209	US 2004-494222		20040503
US 7067543	B2	20060627			
IN 2004CN00973	A	20060203	IN 2004-CN973		20040506
MX 2004PA04390	A	20050516	MX 2004-PA4390		20040507
NO 2004002137	A	20040525	NO 2004-2137		20040525
ZA 200402623	A	20060531	ZA 2004-2623		20060328
PRIORITY APPLN. INFO.:			GB 2001-26901	A	20011108
			GB 2002-12917	A	20020605
			NZ 2002-532587	A3	20021107
			WO 2002-EP12445	W	20021107

OTHER SOURCE(S): MARPAT 138:368777

GI



I



II

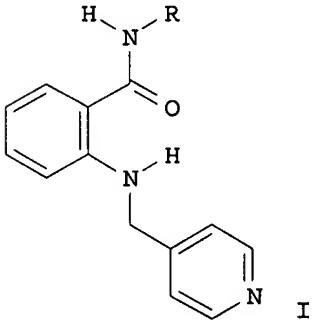
AB The title compds. [I; Ar = II (wherein Ra = H, alkyl; and R1 = H, perfluoroalkyl; R2 = H, halo, alkyl, alkenyl, alkynyl); or Ar = 4-pyridyl and R1 = perfluoroalkyl; R2 = Br, I, alkyl, alkenyl, alkynyl; or R1 = H, and R2 = F, Br, I, Et, alkyl, alkenyl or alkynyl] and their N-oxides and salts, useful for the treatment especially of a neoplastic disease, such as a tumor disease, of retinopathy or age-related macular degeneration in the human or animal body, were prepared and formulated. Thus, reductive amination of 4-pyridinecarboxaldehyde with 2-amino-N-(4-bromo-3-trifluoromethylphenyl)benzamide (preparation given) in the presence of NaBH3CN afforded I [Ar = 4-pyridyl; R1 = CF3; R2 = Br]. The IC50-values that can be found for the compds. I are in range of 0.001 to 1 μM in test for activity against VEGF-receptor tyrosine kinase.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS

Updated Search

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 10 OF 16 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:880425 HCAPLUS
DOCUMENT NUMBER: 138:106488
TITLE: Anthranilic Acid Amides: A Novel Class of Antiangiogenic VEGF Receptor Kinase Inhibitors
AUTHOR(S): Manley, Paul W.; Furet, Pascal; Bold, Guido; Brueggen, Josef; Mestan, Juergen; Meyer, Thomas; Schnell, Christian R.; Wood, Jeanette; Haberey, Martin; Huth, Andreas; Krueger, Martin; Menrad, Andreas; Ottow, Eckhard; Seidelmann, Dieter; Siemeister, Gerhard; Thierauch, Karl-Heinz
CORPORATE SOURCE: Oncology Research, Novartis Pharma AG, Basel, CH-4057, Switz.
SOURCE: Journal of Medicinal Chemistry (2002), 45(26), 5687-5693
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:106488
GI



I

AB Two readily synthesized anthranilamide, VEGF receptor tyrosine kinase inhibitors have been prepared and evaluated as angiogenesis inhibitors. 2-[(4-Pyridyl)methyl]amino-N-[3-(trifluoromethyl)phenyl]benzamide [I; R = 3-CF3C6H4 (II)] and N-3-isoquinolinyl-2-[(4-pyridinylmethyl)amino]benzamide [I; R = 3-isoquinolinyl (III)] potently and selectively inhibit recombinant VEGFR-2 and VEGFR-3 kinases. As a consequence of their physicochem. properties, these anthranilamides readily penetrate cells and are absorbed following once daily oral administration to mice. Both II and III potently inhibit VEGF-induced angiogenesis in an implant model, with ED50 values of 7 mg/kg. In a mouse orthotopic model of melanoma, II and III potently inhibited both the growth of the primary tumor as well as the formation of spontaneous peripheral metastases. The anthranilamides II and III represent a new structural class of VEGFR kinase inhibitors, which possess potent antiangiogenic and antitumor properties.
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 11 OF 16 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:304375 HCAPLUS

Updated Search

DOCUMENT NUMBER: 138:49187
TITLE: CGP 79787D (PTK787/ZK222584), CGP 84738, NVP-AAC789, NVP-AAD777, and related 1-anilino-(4-pyridylmethyl)phthalazines as inhibitors of VEGF- and bFGF-induced angiogenesis
AUTHOR(S): Bold, Guido; Frei, Jorg; Furet, Pascal; Manley, Paul W.; Bruggen, Josef; Cozens, Robert; Ferrari, Stefano; Hofmann, Francesco; Martiny-Baron, Georg; Mestan, Jurgen; Meyer, Thomas; Wood, Jeanette M.
CORPORATE SOURCE: Oncology Research, Novartis Pharma AG, Basel, CH-4002, Switz.
SOURCE: Drugs of the Future (2002), 27(1), 43-55
CODEN: DRFUD4; ISSN: 0377-8282
PUBLISHER: Prous Science
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. The pharmacol. profile of the class of 1-anilino-(4-pyridylmethyl)-phthalazines is presented. 1-Anilino-(4-pyridylmethyl)phthalazines are potent, selective and orally well absorbed inhibitors of vascular endothelial growth factor (VEGF) receptor tyrosine kinases. In vitro they block VEGF-stimulated autophosphorylation of KDR expressing cells, resulting in the inhibition of survival effects of VEGF on endothelial cells. They also block platelet derived factor-mediated effects at slightly higher concentration but do not affect other pathways such as the bFGF receptor.
REFERENCE COUNT: 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 12 OF 16 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:803259 HCAPLUS
DOCUMENT NUMBER: 137:15067
TITLE: Tyrosine kinase inhibitors: From rational design to clinical trials
AUTHOR(S): Traxler, Peter; Bold, Guido; Buchdunger, Elisabeth; Caravatti, Giorgio; Furet, Pascal ; Manley, Paul; O'Reilly, Terence; Wood, Jeanette; Zimmermann, Juerg
CORPORATE SOURCE: Novartis Pharma AG, Basel, CH-4002, Switz.
SOURCE: Medicinal Research Reviews (2001), 21(6), 499-512
CODEN: MRREDD; ISSN: 0198-6325
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Protein kinases play a crucial role in signal transduction as well as in cellular proliferation, differentiation, and various regulatory mechanisms. The inhibition of growth related kinases, especially Tyr kinases, might provide new therapies for diseases such as cancer. The progress made in the crystallization of protein kinases has confirmed that the ATP-binding domain of Tyr kinases is an attractive target for drug design. Three successful examples of drug design at Novartis using a Tyr kinase as a mol. target are described. PK1166, a pyrrolo[2,3,-d]pyrimidine derivative, is a dual inhibitor of both the EGFR and the ErbB2 kinases. The compound entered clin. trials in 1999, based on its favorable pre-clin. profile: potent inhibition of EGF-mediated signalling in cells, in vivo antitumor activity in several EGFR over-expressing xenograft tumor models in nude mice, long-lasting inhibition of EGF-stimulated EGFR auto-phosphorylation in tumor tissue, good oral bioavailability in animals, and no prohibitive in vitro and in vivo toxicity findings. The anilino-phthalazine derivative

Updated Search

PTK787/ZK222584 (Phase I, co-developed by Schering AG, Berlin) is a potent and selective inhibitor of both the KDR and Flt-1 kinases with interesting anti-angiogenic and pharmacokinetic properties (orally bioavailable). STI 571 (Glivec, Gleevec), a phenylamino-pyrimidine derivative, is a potent inhibitor of the Abl Tyr kinase, which is present in 95% of patients with chronic myelogenous leukemia (CML). The compound specifically inhibits proliferation of v-Abl and Bcr-Abl expressing cells (including cells from CML patients) and shows anti-tumor activity as a single agent in animal models at well-tolerated doses. Pharmacol. relevant concns. are achieved in the plasma of animals (oral administration). Promising data from phase I and II clin. trials in CML patients (98% hematol. response rate in Phase I) support the fact that the STI571 represents a new treatment modality for CML. In addition, potent inhibition of the PDGFR and c-Kit Tyr kinases also indicates its possible clin. use in solid tumors.

REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 13 OF 16 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:509389 HCAPLUS
DOCUMENT NUMBER: 134:216785
TITLE: New anilinophthalazines as potent and orally well absorbed inhibitors of the VEGF receptor tyrosine kinases useful as antagonists of tumor-driven angiogenesis. [Erratum to document cited in CA133:99079]
AUTHOR(S): Bold, Guido; Altmann, Karl-Heinz; Frei, Joerg; Lang, Marc; Manley, Paul W.; Traxler, Peter; Wietfeld, Bernhard; Brueggen, Josef; Buchdunger, Elisabeth; Cozens, Robert; Ferrari, Stefano; Furet, Pascal; Hofmann, Francesco; Martiny-Baron, Georg; Mestan, Juergen; Roesel, Johannes; Sills, Matthew; Stover, David; Acemoglu, Figan; Boss, Eugen; Emmenegger, Rene; Laesser, Laurent; Masso, Elvira; Roth, Rosemarie; Schlachter, Christian; Vetterli, Werner; Wyss, Dominique; Wood, Jeanette M.
CORPORATE SOURCE: Oncology Research and Process Research, NOVARTIS Pharma AG, Basel, CH-4002, Switz.
SOURCE: Journal of Medicinal Chemistry (2000), 43(16), 3200
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB On page 2316, in Table 3, the unit for cmax; the concentration should be given as
[μM]. The correct version of Table 3 is given.

L12 ANSWER 14 OF 16 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:359936 HCAPLUS
DOCUMENT NUMBER: 133:99079
TITLE: New Anilinophthalazines as Potent and Orally Well Absorbed Inhibitors of the VEGF Receptor Tyrosine Kinases Useful as Antagonists of Tumor-Driven Angiogenesis
AUTHOR(S): Bold, Guido; Altmann, Karl-Heinz; Frei, Joerg; Lang, Marc; Manley, Paul W.; Traxler, Peter; Wietfeld, Bernhard; Brueggen, Josef; Buchdunger, Elisabeth; Cozens, Robert; Ferrari, Stefano; Furet, Pascal; Hofmann, Francesco; Martiny-Baron, Georg; Mestan, Juergen; Roesel, Johannes; Sills, Matthew; Stover, David; Acemoglu,

Updated Search

Figan; Boss, Eugen; Emmenegger, Rene; Laesser, Laurent; Masso, Elvira; Roth, Rosemarie; Schlachter, Christian; Vetterli, Werner; Wyss, Dominique; Wood, Jeanette M.

CORPORATE SOURCE: Oncology Research and Process Research, NOVARTIS Pharma AG, Basel, CH-4002, Switz.

SOURCE: Journal of Medicinal Chemistry (2000), 43(12), 2310-2323
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The sprouting of new blood vessels, or angiogenesis, is necessary for any solid tumor to grow large enough to cause life-threatening disease. Vascular endothelial growth factor (VEGF) is one of the key promoters of tumor induced angiogenesis. VEGF receptors, the tyrosine kinases Flt-1 and KDR, are expressed on vascular endothelial cells and initiate angiogenesis upon activation by VEGF. 1-Anilino-(4-pyridylmethyl)-phthalazines, such as CGP 79787D (or PTK787 / ZK222584), reversibly inhibit Flt-1 and KDR with IC50 values < 0.1 μM. CGP 79787D also blocks the VEGF-induced receptor autophosphorylation in CHO cells ectopically expressing the KDR receptor (ED50 = 34 nM). Modification of the 1-anilino moiety afforded derivs. with higher selectivity for the VEGF receptor tyrosine kinases Flt-1 and KDR compared to the related receptor tyrosine kinases PDGF-R and c-Kit. Since these 1-anilino-(4-pyridylmethyl)phthalazines are orally well absorbed, these compds. qualify for further profiling and as candidates for clin. evaluation.

REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 15 OF 16 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:335388 HCAPLUS
DOCUMENT NUMBER: 132:347491

TITLE: Preparation of N-aryl(thio)anthranilic acid amides as VEGF receptor tyrosine kinase inhibitors

INVENTOR(S): Altmann, Karl-Heinz; Bold, Guido; Furet, Pascal; Manley, Paul William; Wood, Jeanette Marjorie; Ferrari, Stefano; Hofmann, Francesco; Mestan, Jurgen; Huth, Andreas; Kruger, Martin; Seidelmann, Dieter; Menrad, Andreas; Haberey, Martin; Thierauch, Karl-Heinz

PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis-Erfindungen Verwaltungsgesellschaft m.b.H.; Schering Aktiengesellschaft
SOURCE: PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000027820	A1	20000518	WO 1999-EP8545	19991108

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,

Updated Search

CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

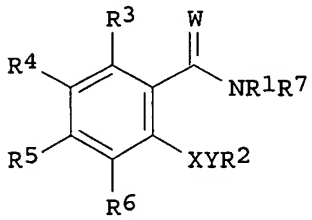
CA 2346898	A1	20000518	CA 1999-2346898	19991108
BR 9915210	A	20010724	BR 1999-15210	19991108
TR 200101237	T2	20010821	TR 2001-200101237	19991108
EP 1129075	A1	20010905	EP 1999-971802	19991108
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
HU 200104188	A2	20020328	HU 2001-4188	19991108
JP 2002529453	T	20020910	JP 2000-581000	19991108
AU 758230	B2	20030320	AU 2000-13811	19991108
NZ 511339	A	20030725	NZ 1999-511339	19991108
RU 2286338	C2	20061027	RU 2001-114978	19991108
NO 2001001894	A	20010704	NO 2001-1894	20010417
ZA 2001003290	A	20030123	ZA 2001-3290	20010423
MX 2001PA04256	A	20030606	MX 2001-PA4256	20010427
US 2002019414	A1	20020214	US 2001-850434	20010507
US 6448277	B2	20020910		
IN 2001CN00638	A	20050304	IN 2001-CN638	20010508
ZA 2001004673	A	20020909	ZA 2001-4673	20010607
US 2003064992	A1	20030403	US 2002-180289	20020626
US 6878720	B2	20050412		
US 2004198782	A1	20041007	US 2004-828951	20040421
US 7002022	B2	20060221		
US 2006074112	A1	20060406	US 2005-254897	20051020

PRIORITY APPLN. INFO.:

GB 1998-24579	A	19981110
WO 1999-EP8545	W	19991108
US 2001-850434	A3	20010507
US 2002-180289	A3	20020626
US 2004-828951	A3	20040421

OTHER SOURCE(S): MARPAT 132:347491

GI



I

AB Use of title compds. I; W = O, S; X = NR8; Y = CR9R10(CH2)n, SO2; R9, R10 = H, alkyl; n = 0-3; R1 = aryl; R2 = mono- or bicyclic heteroaryl with the exception that R2 cannot = 2-phthalimidyl, and when Y = SO2 cannot represent 2,1,3-benzothiadiazol-4-yl; R3-R6 = H, substituent; R7, R8 = H, alkyl; or a N-oxide or a pharmaceutically acceptable salt thereof, for the preparation of a pharmaceutical product for the treatment of a neoplastic disease which responds to an inhibition of the VEGF receptor tyrosine kinase activity is claimed. Thus, a mixture of 4-pyridinecarboxaldehyde and 2-amino-N-(4-trifluoromethylphenyl)benzamide (preparation given) in MeOH containing HOAc was treated with NaBH3CN followed by 16 h stirring to give 2-[(4-pyridyl)methyl]amino-N-[4-(trifluoromethyl)phenyl]benzamide. Tested I inhibited Flt-1 VEGF receptor tyrosine kinase with IC50 = 0.18-0.56 μM.

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

Updated Search

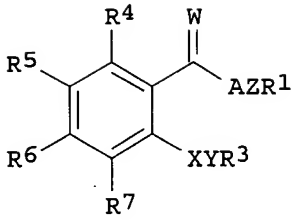
L12 ANSWER 16 OF 16 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:335387 HCAPLUS
DOCUMENT NUMBER: 132:334364
TITLE: Preparation of anthranilic acid amides as vascular endothelial growth factor receptor inhibitors.
INVENTOR(S): Huth, Andreas; Seidelmann, Dieter; Thierauch, Karl-Heinz; Bold, Guido; Manley, Paul William; Furet, Pascal; Wood, Jeanette Marjorie; Mestan, Jurgen; Bruggen, Jose; Ferrari, Stefano; Kruger, Martin; Ottow, Eckhard; Menrad, Andreas; Schirner, Michael
PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany; Novartis Aktiengesellschaft
SOURCE: PCT Int. Appl., 96 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000027819	A2	20000518	WO 1999-EP8478	19991109
WO 2000027819	A3	20000817		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19910396	A1	20000907	DE 1999-19910396	19990303
DE 19910396	C2	20011213		
CA 2350208	A1	20000518	CA 1999-2350208	19991109
BR 9915553	A	20010814	BR 1999-15553	19991109
EP 1129074	A2	20010905	EP 1999-953967	19991109
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
HU 200104425	A2	20020328	HU 2001-4425	19991109
TR 200101307	T2	20020521	TR 2001-200101307	19991109
JP 2002529452	T	20020910	JP 2000-580999	19991109
EE 200100258	A	20021216	EE 2001-258	19991109
NZ 511413	A	20040130	NZ 1999-511413	19991109
AU 771180	B2	20040318	AU 2000-10454	19991109
IN 2001MN00422	A	20060203	IN 2001-MN422	20010419
NO 2001002245	A	20010710	NO 2001-2245	20010507
NO 320647	B1	20060109		
MX 2001PA04692	A	20020311	MX 2001-PA4692	20010509
BG 105588	A	20020430	BG 2001-105588	20010611
US 7122547	B1	20061017	US 2001-831506	20010914
HK 1041882	A1	20050318	HK 2002-103628	20020514
IN 2005MN00687	A	20051007	IN 2005-MN687	20050628

PRIORITY APPLN. INFO.:	GB 1998-24579	A	19981110
	DE 1999-19910396	A	19990303
	WO 1999-EP8478	W	19991109
	IN 2001-MN422	A3	20010419

OTHER SOURCE(S): MARPAT 132:334364
GI

Updated Search



I

AB Title compds. [I; A = NR2; W = O, S, H2, NR8; Z = NR10, N, NR10(CH2)q, alkyl, etc.; q = 1-6; AZR1 = tetrahydroisoquinolinyl, indazolyl, 5-chloroindolyl, etc.; R1 = (substituted) aryl, heteroaryl; R2 = H, alkyl; R3 = (substituted) mono- or bicyclic aryl, heteroaryl; R4-R7 = H, halo, (substituted) alkoxy, alkyl, carboxyalkyl; R5R6 = dioxetanyl; R8, R10 = H, alkyl]. Thus, Me N-(4-pyridylmethyl)anthranilate (preparation given) was stirred with Ph(CH2)3NH2 and Me3Al were stirred in PhMe to give N-(3-phenylprop-1-yl)-N2-(4-pyridylmethyl)anthranilamide. The latter inhibited VEGFR I with IC50 = 0.05 μM.

Updated Search